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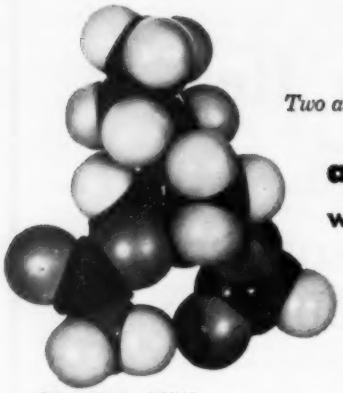

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A Comparison of Chlorpromazine and Reserpine in Chronic Psychosis

B. KOVITZ, M.D.
J. T. CARTER, Ph.D.
and
W. P. ADDISON, M.D., Columbus, Ohio

The growing use of chlorpromazine and reserpine arouses interest in the following questions: 1. How effective are these drugs in chronic psychosis, particularly schizophrenia? 2. In what syndromes are they most useful? 3. What is there relation to other methods of treatment? 4. What are their comparative advantages and disadvantages?

We have tried to gather information on these points by the following procedures:

1. Treatment of patients whose mental illness has resisted other therapies
2. Comparison of the results obtained with the two drugs
3. Control of the findings through the use of placebos
4. Measurement of drug effectiveness by (*a*) behavior ratings, (*b*) concurrent need for ECT (electric convulsive therapy), (*c*) electroencephalographic studies, and (*d*) psychological tests
5. Correlation of the results with the psychiatric syndrome
6. Observation of the effects on psychotherapy

MATERIAL AND METHOD

Our basic study was conducted on 150 patients, with an average time since hospital admission of 6.6 years per patient. All were cases whose illness had not responded well to the usual treatment methods. Half the cases had required maintenance ECT during the seven months preceding the study. The total group included 127 cases of chronic schizophrenia. The remainder consisted of cases of chronic or relapsing manic psychosis, depressive psychoses, and chronic brain syndrome with affective or convulsive disorder.

The 150 patients were divided into three matched groups of 50 (25 of each sex). Group A received placebos throughout the 16-week experiment. Group B received reserpine for six weeks, placebos for four weeks, and chlorpromazine for six weeks. Group C concurrently received chlorpromazine for six weeks, placebos for four weeks, and reserpine for six weeks. Reserpine was used in doses of 2 to 5 mg. daily. Chlorpromazine was used in doses of 100 to 400 mg. daily, except in a small number of cases in which up to 650 mg. was given daily. ECT was suspended, with the understanding that the ward physician could apply it whenever he considered the patient disturbed enough to make it necessary. This arrangement made the need for ECT an inverse measure of drug effectiveness. Behavior was rated each week by attendants, nurses, and physicians, who did not know which medication their patients were receiving.

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Clinical Improvement.—The number of patients showing clinical improvement is listed in Table 1.

The number of patients who have been released from the hospital is as follows: one from the placebo group (2%), five from Group B (10%), and six from Group C (12%).

Received for publication June 21, 1955.

TABLE 1.—*Incidence of Clinical Improvement*

	First 6 Weeks	Second 6 Weeks	12-Week Treatment Period
Group A (placebo).....	11 (22%)	7 (14%)	12 (24%)
Group B.....	24 (48%)	28 (56%)	..
Group C.....	30 (60%)	29 (58%)	..
Cases on reserpine.....	24 (48%)	29 (58%)	53 (53%)
Cases on chlorpromazine	30 (60%)	28 (56%)	58 (58%)

Electroconvulsive Therapy. — ECT requirements before and during the experiment are listed in Table 2.

During the 12 weeks of actual medication, 10 patients in the placebo group required 35 ECT's. In comparison, eight cases on reserpine required a total of 12 ECT's, and eight cases on chlorpromazine required a total of 11 ECT's. This difference between the placebo and the medication groups is at better than the 1% level of significance (occurrence by chance could be less than 1 time in 100) according to the χ^2 test.

Intelligence Scores.—Fifty-four patients cooperated in a complete Wechsler-Bellevue Intelligence Scale. These patients were each tested twice, once after approximately five weeks on medication and once while off medication.

Two methods were used to control the effects of practice and the use of two alternate test forms: 1. Half the patients were given their first test prior to medication and their second test while on the medication. The other half took their first test while on medication and their second test from four to six weeks after the medication period. 2. Half the patients in each series took Wechsler-Bellevue Form I the first time and Form II (an equivalent alternate test) the second time. The other half in each series took Form II the first time and Form I the second time.

TABLE 2.—*Electroconvulsive Therapy Requirements Before and During Experiment*

	7 Months Before Experiment	First 6 Weeks	4 Weeks on Placebo	Second 6 Weeks
Group A				
Cases treated	25	10	7	5
No. of ECT's	334	21	12	14
				(on chlorpromazine)
Group B		(on reserpine)		
Cases treated	25	5	7	5
No. of ECT's	350	7	15	7
		(on chlorpromazine)		
Group C				(on reserpine)
Cases treated	24	3	4	3
No. of ECT's	287	4	4	5

TABLE 3.—*Wechsler-Bellevue Intelligence Scores*

	Placebo Group (20 Cases)	Reserpine Group (16 Cases)	Chlorpromazine Group (18 Cases)
Not on medication.....	80	90	89
On medication.....	78	94	94
Difference in favor of medication	− 2	− 2	+ 5

The average scores obtained by the three groups are presented in Table 3.

In spite of the use of the alternate test forms, the placebo group showed a slight gain in scores (averaging 2 points) on retesting. This gain may have been the result of better functioning in the retest situation, in which the patients' increased familiarity with the tester enabled them to feel more secure. Although this familiarity variable was scarcely anticipated, it is controlled by the use of the counterbalanced order of testing described above.

The notable finding here is the 5-point average increase in scores during chlorpromazine therapy. The mean difference of the chlorpromazine group scores while on and off the drug was compared statistically with this difference for the placebo group and found to be significant at the 1% level (again indicating that a difference of this size could have occurred due to chance alone less than 1 time in 100).

Electroencephalography. — Three electroencephalograms were obtained for each patient on 34 members of Group A, 25 of Group B, and 26 of Group C. The first record was obtained prior to medication: the second record, during the first six weeks on medication, and the third record, during

TABLE 4.—*Degrees of Muscle Tension Artifact*

	Cases from Group A (Placebo)		Cases from Groups B and C		
Degree of Artifact	Before Medication	Average of Retests	Before Medication	Retest on Reserpine	Retest on Chlorpromazine
4+	2	2.5	6	1	1
3+	12	5.5	6	6	4
2+	9	12	16	9	11
1+	8	9.5	16	24	27
0	3	4.5	7	11	8
	34	34	51	51	51

the last six weeks on medication. The records were rated (1) according to the degree of abnormality and (2) according to the amount of muscle tension artifact. Artifact was rated on a 5-point scale, from 0 to 4+.

There was no significant change in the number of normal and abnormal records on retesting with either placebo or medication. However, on medication a trend appeared toward fewer cases with the higher degrees of muscle tension artifact.

The number of cases with higher amounts (2+ to 4+) of artifact decreased from 67% to 59% in the group of placebos, whereas the number of cases with higher amounts of artifact decreased from 55% to 31% with either reserpine or chlorpromazine.

Blood Studies.—Blood counts and serum bilirubin, alkaline phosphatase, thymol turbidity, and serum mucoprotein studies were obtained on two-thirds of the experimental group. The most complete and significant set of retest data was obtained on serum bilirubin in Group C following the course of chlorpromazine. The average serum bilirubin readings are summarized in Table 5.

TABLE 5.—*Serum Bilirubin Readings with Chlorpromazine*

No. of Tests	Averaged Initial Readings	Time of Retest (Weeks After Chlorpromazine)	Averaged Retest Readings
38	0.543	0-2	1.984
13	0.312	3-4	1.615
6	0.741	5-6	1.083
16	0.365	7-8	0.325

The pattern is a distinct rise in serum bilirubin after six weeks on chlorpromazine, followed by a steady decline to the original levels in the six to eight weeks after the medication was stopped.

QUALITATIVE OBSERVATIONS

These comments are derived from clinical experience with approximately 250 cases in addition to the 150 on which our quantitative data are based. We are not presenting this experience in anecdotal detail but wish to summarize our impressions as clinical hypotheses clearly open to revision.

A. Observations Applicable to Both Chlorpromazine and Reserpine

Patients with chronic psychosis of many years' duration may improve with either chlorpromazine or reserpine. When improvement is obtained, it is usually shown by (*a*) less intense or impulsive expression of emotion and (*b*) increased interest and adaptiveness in social interaction.

In cases of chronic schizophrenia the results are much less spectacular than in acute cases. The benefits are often noted simply as less disturbance or as less need for somatic therapy. Attendants often did not fully appreciate the subtle change in the patients until the latter were on placebos, when the return to more disturbed behavior became apparent.

In every instance, the basic personality disorder could be readily demonstrated regardless of the degree of symptom improvement. In no sense could the results be considered as cure or disappearance of the mental illness.

Benefits were minimal in cases showing advanced schizophrenic "deterioration," with intellectual and emotional inaccessibility. Benefits were maximal in cases showing persistent tension, hostility, attitudes of self-justification, and efforts to maintain some type of communication and social status. Put in diagnostic terms, the patients with schizoaffective, acute undifferentiated, catatonic, and paranoid schizophrenia are apt to be better subjects than those with the chronic, simple, and hebephrenic forms. The duration and diagnosis of the illness are of less prognostic importance than the presence of tension and compensatory strivings for self-esteem. Benefit has been impressive in patients without much deterioration whose previous efforts to live outside the hospital had repeatedly been foiled by episodes of intolerable tension. In such instances, the use of these medications has made a critical difference through helping the patient to handle life and work situations with an adequacy hitherto impossible.

The motor-affective and behavioral component of the disorder is influenced much

sooner and more readily than is the ideational component. Manics, who generally responded with decreased hyperactivity and talkativeness, continued for some time to display a manic type of thinking and impairment of judgment. Schizophrenics have continued to show delusional, hallucinative, or obsessive experiences after the emotional intensity of their response had distinctly subsided.

In our experience, ECT has been safely combined with reserpine or chlorpromazine by using a lower than usual current dose. The ECT effects seem to be enhanced, and a smaller number of treatments appears effective. ECT is still necessary in cases of depression, which may even appear intensified as anxious tension diminishes.

The drugs have not interfered with psychotherapy, and in a number of instances have had a favorable influence. Some patients have shown a spontaneous shift from "delusional" to "realistic" preoccupations, even though the increase in formal insight was minor. Thinking and associations have become clearer and more relevant. In particular, the tension-damping effect has permitted some patients to manifest and verbalize strong feelings, especially hostile feelings, without a catastrophic loss of control. This has been a constructive experience for persons who could not previously handle their psychotically intense affect. In one case in which disturbed episodes still occurred, but were scaled down to manageable size by reserpine, rather than obscured by ECT, there has been a visible improvement in insight and cooperation.

It is extremely important not to forget the meaning of the illness in our enthusiasm over a new symptomatic remedy. When medication has been used exclusively for symptom or affect suppression, the results have been disappointing and sometimes disastrous. Symptomatic improvement must not be mistaken for a genuine resolution of the patient's difficulties. Although the mere decrease of tension may be a great aid in freeing a person's potentialities for living, we must not overlook the function of the symptom as the only available expression of a serious unsolved problem in the patient's life. Where the problem is forgotten in our eagerness for dramatic results, it is only too apt to make its reappearance through distressing relapses, and even attempts at suicide.

B. Observations Applicable to Reserpine

1. Results are obtained much more slowly with reserpine than with chlorpromazine. In severe psychotics, an intramuscular dose of 5 to 10 mg. for days has been a valuable or necessary preliminary to good results. Patients have shown gradual improvement in the course of three to six months or longer on oral medication. Supplementary intramuscular medication has been of value in dealing with relapses or recurrent "disturbed" phases.

2. Subjectively unpleasant side-effects are often more evident than with chlorpromazine. Many patients have to go through a definite adaptation period of several weeks before they can comfortably tolerate an effective dose. One patient who originally could hardly tolerate 0.125 mg. a day has finally derived real benefit from 4 mg. a day. With patient manipulation of dosage it is rare for complications to compel discontinuance of the drug.

3. The most specific effect attributable to reserpine has been its capacity to diminish the intensity of pathological emotions, rather than to change their character. The anxiety or hostility is likely to become moderated or limited rather than to disappear. The patient does not usually appear essentially different; he tends to be better controlled, holds up better under pressure, and tends to shift to a less psychotic mode of adjustment.

C. Observations Applicable to Chlorpromazine

1. Results are often rapid and obvious once an adequate dose of chlorpromazine is reached. Exceptionally, patients have required up to 600 mg. a day. Most patients have shown improvement with 150 to 400 mg. daily and may maintain the improvement as the dose is gradually lowered.

Abrupt termination often leads to tenseness or relapse.

2. Subjectively unpleasant side-effects are less in evidence than with reserpine. The patient is sometimes consciously grateful for the relief of physical tension. However, objective complications, such as skin eruptions, have forced interruption of the medication in about 5% of our cases. No overt jaundice has been noted so far.

3. The most specific effect of chlorpromazine is its capacity to diminish anxious or hostile tension. There is often a qualitative shift in affect toward relaxation and friendliness, as well as a quantitative decrease in tension or excitement. It is this property which makes chlorpromazine an outstanding contribution to the treatment of paranoid schizophrenia. Irritable or hostile epileptics have also improved when chloropromazine was added to their anticonvulsant regimen. In patients on psychotherapy the medication favors a useful release of affects and memories.

4. An important limitation of chlorpromazine is its failure to improve depression. Even when the tense or anxious component of a psychotic depression is relieved, the basic depressive mood quickly recurs or continues unabated. We know of four instances in which patients, in spite of showing some tension relief with chlorpromazine, have made suicidal attempts. ECT or other therapeutic measures may be essential in treating such problems.

SUMMARY AND CONCLUSIONS

Improvement was found in 53% of cases of severe chronic schizophrenia treated with reserpine, in 58% of such cases treated with chlorpromazine, and in 24% of similar cases treated with placebos. Placebo cases also required about three times as much electroconvulsive therapy.

ECT may be effectively combined with reserpine or chlorpromazine, and fewer treatments are required to achieve symptomatic benefit.

Chlorpromazine produced a slight, but significant, increase in the intelligence test scores of patients with chronic psychoses, presumably through diminishing anxiety.

Chlorpromazine and reserpine both tended to decrease muscle tension artifact in the EEG.

Chlorpromazine produced a sustained increase in serum bilirubin in many patients without overt jaundice.

Reserpine acts more slowly. Its side-effects are apt to be unpleasant, but seldom serious. It tends to diminish the quantitative intensity of pathological affects, rather than to change them qualitatively.

Chlorpromazine acts more rapidly. Side-effects are less unpleasant but may require stopping the medication. It is relatively ineffective in depression. It tends to induce qualitative and quantitative improvement in states of anxiety, tension, and hostility.

Chlorpromazine and reserpine produce essentially symptomatic improvement through less intense or impulsive expression of emotion; they influence the motor-affective more readily than the ideational sphere.

Results with these drugs are best in patients with persistent evidence of tension, strong affect, and efforts to maintain self-esteem.

Symptomatic use of these drugs cannot replace adequate therapeutic attention to the patient's underlying problems.

The opportunity to release emotion with less anxiety or impulsiveness is advantageous for psychotherapy with psychotics.

Both drugs are of particular value for the patient with chronic, relapsing, but non-deteriorating schizophrenia who could not otherwise adjust successfully outside the hospital.

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Clarification of the Problem of Vertebral Fractures from Convulsive Therapy

I. Incidence

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REVIEW OF LITERATURE

The problem of clinically significant skeletal complications resulting from convulsive therapy continues to warrant careful study. This has been amply substantiated within the past three years by the development of new muscle-relaxant drugs [1] and the necessity for standards relating to medicolegal aspects.* It is our purpose in this section of our paper to review the literature relating to the incidence of such complications, with special reference to vertebral fractures. The emphasis on vertebral fractures is dictated by the wealth of material, the wide range in reported incidence, and the apparent lack of agreement in discussions relating to mechanisms of production and methods of prevention. In contrast, there are relatively few studies dealing with the incidence of other skeletal complications. Perhaps the problem here is clear cut. Dislocations and fractures (other than vertebral) are generally diagnosed with less difficulty and usually necessitate immediate treatment, and the clinical significance is unquestioned. There is scant mention of injuries to muscles, tendons, and joints in the literature. Although probably frequent, they defy clear-cut diagnosis and are rarely considered to be of clinical significance unless associated with fractures or dislocations.

A general survey of the literature relating to vertebral fractures suggested the possible value of more detailed consideration of the following studies: (1) those reporting incidence on a statistical basis and (2) those dealing with factors possibly responsible for incidence. The facts herein are well known, but, understandably, they are usually considered selectively and briefly as introductory material in any one study. More comprehensive review suggests several general trends, which may serve to clarify in part the clinical approach to the problem. Further studies will deal with clinical aspects of the problem as suggested in this review, and will be based on clinical experience and roentgenological survey of vertebral fractures resulting from electroconvulsive therapy (ECT) at this hospital.

STATISTICAL REPORTS

Injuries to Muscles, Tendons and Joints.—Statistical studies are not available. According to Kalinowsky and Hoch,[4] these structures are "rarely injured," and the difficulties of differential diagnosis are held chiefly responsible. It is tempting to speculate that such injuries are frequently responsible for subjective complaints of pain unaccompanied by recognizable skeletal damage. It is probably of far greater benefit therapeutically, however, to understand the subjective pain in terms of dynamic meaning for the individual patient.

Dislocations: The joints most frequently involved are the jaw, shoulder, and elbow. There are few statistical studies available.

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* References 2 and 3.

Carp,[5] in 1939, reported the over-all incidence of dislocations via pentylenetetrazol (Metrazol) convulsive therapy as 17.2% of cases treated. Deshaies and Pellier,[6] in 1950, reviewed the incidence incurred through electroconvulsive therapy. Based on a study of over 16,000 cases from the literature, jaw dislocations were found to have occurred in 6%, and shoulder dislocations in 0.5%, of reported cases.

Fractures: Likewise, there are relatively few statistical studies dealing with incidence of fractures other than vertebral compression fractures. Cook,[7] in 1944, reviewed the literature and reported comparative figures for the incidence of fracture as follows: (1) epilepsy, 16.8%; (2) Metrazol convulsive therapy, 21.5%, and (3) ECT, 3.9%. The Deshaies and Pellier survey [6] indicated that the bones most frequently involved in ECT are the jaw (0.4% of reported cases), femur (0.2%), neck of the humerus (0.18%), and spine (1.0%). It is noteworthy that Kalinowsky and Hoch [4] also included fractures of the acetabulum and scapula, but these were apparently not of statistical significance, as figures were not reported. In general, Kalinowsky and Hoch [4] emphasized that fractures complicating ECT are "rare" and "unpredictable."

Vertebral Compression Fractures: The literature in this area is voluminous. Well over 100 reports were reviewed for this study. Forty of these were selected for more detailed study (Table 1). The studies included relate to insulin coma therapy, Metrazol convulsive therapy, and ECT. Although insulin coma therapy is not routinely considered "convulsive" therapy, it is well known that spontaneous generalized motor convulsions occur during the course of treatment. Frequently clonic or tonic spasms are severe enough to suggest the possibility of resultant vertebral fracture. In all of the selected studies convulsive therapy was given without a muscle-relaxant drug. The use of muscle-relaxant drugs, routinely or in selected cases, is per se a major area for investigation. All of the studies reported have been published in English. This limitation was arbitrarily set, as pertinent studies appearing in French, German, Russian, and Italian journals are not readily available. It will be noted in Table 1 that the statistical reports have been classified on the basis of routine x-ray examination. In the first group of papers, the term "None" indicates that x-rays of the spine were not made. Diagnosis of vertebral compression fractures was based on clinical examination alone. In the second group, the term "Inconsistent" indicates that x-rays were made routinely, but not routinely before and after the series of treatments. In some cases x-rays were taken only if the patient complained of back pain. In other cases x-rays were taken routinely prior to convulsive therapy, and thereafter only if the patient complained of pain. In still other studies x-rays were taken routinely only after the patient had completed the course of therapy. In the third group of papers, the term "Pre- and post-therapy" indicates that x-rays were taken routinely prior to and after the series of convulsive treatments. "Span" indicates the interval of time during which the studies were published. The number of "Cases" represents the total reported in all studies under consideration. For example, in eight ECT studies, with x-ray examination made routinely before and after therapy, a total of 999 cases was reported. The "% Range"

TABLE 1.—*Incidence of Compression Fracture—Survey of Statistical Reports*

Routine X-Rays	Studies	Span	Cases	% Range
		Insulin*		
None	1	1939	1,404	0.0
Inconsistent ...	2	1940	120	20.5-31.4
Pre- and post-therapy	3	1940-1952	102	16.2-33.3
		Metrazol†		
None	1	1939	3,040	0.0
Inconsistent ...	12	1939-1942	1,498	0.0-47.0
Pre- and post-therapy	5	1940-1944	1,110	0.0-42.6
		ECT‡		
None	2	1941-1944	400	0.0
Inconsistent ...	13	1942-1952	6,606	0.5-30.0
Pre- and post-therapy	8	1941-1954	999	0.0-35.4

* References 5 and 8-11.
† References 5, 10, and 12-15.
‡ References 22 and 26-47.

indicates range of incidence on a percentage basis reported in the studies analyzed. For example, within the group of eight studies involving ECT with pre- and post-treatment x-rays, the lowest incidence reported was zero and the highest incidence was 35.4%.

It is perhaps pertinent to relate the incidence of vertebral fractures to the clinical introduction of these therapeutic agents. The first reports of insulin coma therapy appeared in 1933,[48] but vertebral fractures were not reported as a complication until 1940.[9] Initial clinical reports on the use of Metrazol convulsive therapy appeared in 1935,[49] but it was not until 1938 that first reports of vertebral fractures appeared.† In the case of ECT, three years (1938-1941) separated initial reports of clinical use [52] and the first study [39] on the basis of clinical examination alone. Furthermore, follow-up studies indicate that neurological and orthopedic sequelae are negligible.‡ Superficially, it would seem that subjective complaint of localized pain following treatment would be a reliable guide to clinical diagnosis. As an indicator of vertebral fracture, however, subjective pain is of questionable value. It is apparent in Table 2 that the percentage of patients who complain of pain and prove to have vertebral fracture may range from zero to 100%. It is also clear that patients may complain of pain and show no x-ray evidence of vertebral fracture.

The data given in Table 1 suggest that routine x-ray examination is essential to diagnosis. It is apparent that if no x-rays are taken the incidence of vertebral fractures

TABLE 2.—*Relation of Subjective Pain and Vertebral Compression Fractures (C. F.)*

G. M. C.* via	Cases Reported	Incidence of C. F.	No. of Cases With Pain	C. F.		C. F., % With Pain	Bibliographic Reference
				With Pain	Without Pain		
Metrazol	17	47.0%	8	8	0	100%	14
Metrazol	65	18.5%	1	0	11	0	18
Metrazol	75	42.6%	32	20	19	62.5%	23
ECT	212	35.4%	13	8		61.5%	44
ECT	85	27.0%	12	6	6	50%	W. P. I.†

* G. M. C. indicates grand mal convulsions.
† Western Psychiatric Institute and Clinics.

referring to vertebral fracture as a complication. Initial enthusiasm routinely attends the introduction of any new—and relatively effective—therapeutic agent. This often tends to mask the recognition of complications. It is probably of greater significance, however, that clinical diagnosis of vertebral fractures is exceedingly difficult unless there are objective signs of neurological and/or orthopedic damage. Such damage is almost always observed in the case of traumatic vertebral fractures encountered by the orthopedist. It is probable that the clinical significance of vertebral fractures resulting from convulsive therapy is frequently evaluated on this basis. Actually, by far the greater number of vertebral fractures resulting from convulsive therapy are subjectively asymptomatic, and objectively without sign of structural change is comfortably zero. Two Metrazol studies, both published in 1939, illustrate the extremes. In one study,[5] involving 3000 cases, no x-rays were taken and the incidence of vertebral compression fractures was zero. In the second study,[15] reporting 51 cases, x-rays were taken routinely after treatment and the incidence was 43.1%. This not only suggests that x-rays are essential to diagnosis but also serves to substantiate the impression that clinical diagnosis, per se, is an unreliable guide.

Assuming at this point that x-ray examination is essential to adequate diagnosis, it is interesting to note that it seems to make little difference, statistically speaking, whether x-rays are taken "inconsistently" or routinely before and after therapy (Table 3). The range of incidence reported for each thera-

† References 50 and 51.

‡ References 19, 25, 41, 53, and 54.

TABLE 3.—*Effect of Routine X-Ray Examination on Incidence of Vertebral Compression Fracture*

X-Ray	Insulin Coma	Metrazol	ECT
Inconsistent	20.5-31.4	0-47.0	0.5-30.0
Pre- and post-therapy..	18-33.3	0-42.6	0-35.4

peutic agent is approximately the same. This, in turn, suggests that film interpretation may be of even greater significance in determining incidence than is the film per se. Film interpretation is in most instances the responsibility of the radiologist, who may or may not participate actively in writing the final report. It is of interest, in this connection, to note the contribution of radiologists to the ECT studies under consideration (Table 4). This does not mean that the x-ray films were not evaluated by qualified roentgenologists. The discrimination here is based on the answer to the following question—Who writes the papers? It is apparent that the majority (75% roughly) were written by psychiatrists. Radiologists authored or co-authored only 5 of the 21 papers considered here. When psychiatrists wrote the papers, the incidence reported was under 20%. When radiologists participated, however, the incidence reported was over 20%. Again, it did not seem to matter whether x-rays were taken "inconsistently" or routinely before and after therapy. This suggests that the more active the participation of the radiologist the higher the incidence of vertebral fractures. This is, of course, valid only as a statistical observation within the limits of study. It is obvious that true incidence can be evaluated only when films made both before and after therapy are available for interpretation. Recognition of vertebral fractures present prior to therapy would not otherwise be possible.

FACTORS RELATING TO INCIDENCE

A survey of the literature in this field suggests that numerous factors may be operating simultaneously to affect the incidence of vertebral fractures resulting from convulsive therapy. Those factors most frequently suggested in the literature are listed in Table 5. The outline suggests that these factors relate primarily to patient, therapist, or radiologist. No attempt will be made to discuss the merits of including a given factor. Nor is it within the scope of this study to determine the relative significance of a given factor. Many of these factors are discussed in the literature on the basis of clinical impression and theoretical consideration. In some cases statistical evaluations are available. Where these have been possible, however, comparative evidence is often conflicting. Studies relating to age, for example, clearly illustrate this. Easton and Sommers,[24] in a study of 200 patients, found the over-all incidence of vertebral compression fracture to be 23%. In patients over 55 and in those under 21 years of age, however, the incidence was significantly greater—57% and 40%, respectively. In another study, by Meschan, Scruggs, and associates,[44] the over-all incidence was 34.4% of 212 patients. A higher incidence (46%), however, was found in those patients 30 to 39 years of age. In two other studies § no correlation was found between incidence and age. Statistical studies relating to sex also illustrate this point (Table 6). Most of the reports indicate that men are more susceptible to vertebral fracture than are women. In five Metrazol studies,‖ reports of incidence for men range from 17.8% to 60%, and for women from 11.4% to 30.9%. In six ECT studies,¶ the range of incidence reported for men is 20.5% to 42.9% and that for women, 0 to 20.0%. This apparently conclusive evidence, however, is contradicted by two Metrazol studies # in which the incidence was found

§ References 10 and 15.
‖ References 19 and 22 to 25.
¶ References 22, 37, and 43 to 45.
# References 14 and 15.

TABLE 4.—*Effect of Participation of Radiologist on Incidence of Vertebral Compression Fracture*

	X-Ray Inconsistent		Pre- and Post-Treatment X-Rays	
	Studies	% Range	Studies	% Range
No radiologist*....	11	0.5-17	5	0-19.4
Radiologist†	2	21.3-30	3	20.8-35.4

* References 28-36, 38-42, 45, and 46.
† References 22, 37, 43, 44, and 47.

TABLE 6.—*Sex Incidence in Vertebral Compression Fractures*

Men More Susceptible?

G. M. C. via	No. of Studies	Men, % C. F.	Women, % C. F.
Metrazol	5	17.8-60	11.4-30.9
ECT	6	20.5-42.9	0-20.0

Women More Susceptible?

Study	Date	G. M. C. via	Men		Women	
			No.	% C. F.	No.	% C. F.
Bennett & Fitzpatrick	1939	Metrazol	3	33⅓%	14	50%
Polatin, Friedman, et al.	1941	Metrazol	20	30%	31	51.6%
W. P. I.*	1953	ECT	20	20%	65	29.2%

* Western Psychiatric Institute and Clinics.

to be higher for women than for men. An interesting question is suggested by Funkhouser and Davis,[45] who found the incidence of vertebral fracture in 154 white men to be 24%, in 61 Negro men to be 14.8%, and in 43 white women to be 11.6%. It is generally suggested that the proportionately larger muscle mass in men is responsible for higher incidence. On the basis of this assumption, however, one would expect Negro men to sustain vertebral fracture as frequently as white men. The evidence in the study by Funkhouser and Davis does not substantiate this. It is probable that multiple factors are interrelated and interdependent. It is notoriously difficult in clinical research to control conditions sufficiently to permit evaluation of an isolated factor. Often, conditions of study are not clearly described. Frequently a wide range of interpretation is possible, because terminology is not strictly defined. With these difficulties in mind it is not surprising that personal experience and clinical impression often seem to yield more valid evidence than the results of scientific investigation.

SUMMARY AND CONCLUSIONS

A general review of the literature relating to the incidence of skeletal complications resulting from convulsive therapy indicates that there are few statistical studies dealing with skeletal complications other than vertebral fractures.

TABLE 5.—*Factors Possibly Related to Incidence of Vertebral Compression Fracture as Reported in the Literature*

Relating to Patient	Relating to Therapist	Relating to Radiologist
Age	Choice of machine	Technical filming difficulties
Sex	Design of stimulus	True lateral view at constant distance
Race	Modifications of use	Difficult to show T 1-2-3 without laminagraph
Nutritional state	Glissando	Frequently uncooperative patient
Mental status	Threshold stimulus	Reading of films
Type of psychosis	Suppression of clonic phase	Definition of C. F.?
Duration of illness	Petit mal to grand mal	Degree of cupping?
Body build	Use of machine by therapist	Degree of wedging?
Adiposity	Position of patient	Technique of estimation
Muscularity	Supine	Observation without actual measurement
Spine	Sitting	Actual measurement and comparison
Normal development	Use of restraint	No. of sequential films for comparison
Anatomy	Supporting surface	
Kinesiology	Bed	
Pathology	Table	
History of previous G. M. C.*	Fixation of position	
G. M. C.,	Hyperextension	
Convulsive pattern	Flexion	
"Jackknife," tonic phase	Manual restraint	
Disc repercussion, clonic phase	Chemical restraint	
	Muscle-relaxant drugs	
	Sedation	

* Grand mal convulsion.

Consideration of 40 statistical studies reporting incidence of vertebral fractures suggests the following generalizations relating to diagnosis:

(*a*) X-ray examination is essential.

(*b*) X-ray examination, per se, is not as important as film interpretation.

(*c*) Clinical examination, without x-ray evidence, is not a reliable guide.

(*d*) Subjective pain is not a reliable indicator.

The degree of active participation of the radiologist in the statistical reporting of vertebral fractures is an important factor in determining the reported incidence.

Numerous factors relating to patient, therapist, and radiologist have been suggested in the literature as possibly contributing to the incidence of vertebral fractures.

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Clarification of the Problem of Vertebral Fractures from Convulsive Therapy

II. Roentgenological Considerations

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It is evident that we must have admission films of the thoracic spine of each patient if we are to evaluate correctly the question of vertebral fractures subsequent to convulsive therapy. Many of the patients will be found to show evidence of old disease or trauma, such as juvenile osteochondritis, degenerative arthritis, senile changes, and, possibly, fractures from accidental injuries or previous convulsive therapy.

Quite often we see a thoracic spine with exaggerated kyphosis (Fig. 1) which involves most of the middle and lower thoracic vertebral bodies. In such a case we think of this as representing the end-result of healed osteochondritis of childhood (kyphosis dorsalis juvenilis, or Calvé's disease of the spine).* The vertebral bodies present anterior wedging, increasing toward the center of the arch, similar to the appearance of a keystone at the apex. The reduction in vertical height of each involved vertebra is gradual in such cases, not exceeding 2 mm. This condition is to be differentiated from frank compression fractures (C. F.), which usually do not involve so many segments.

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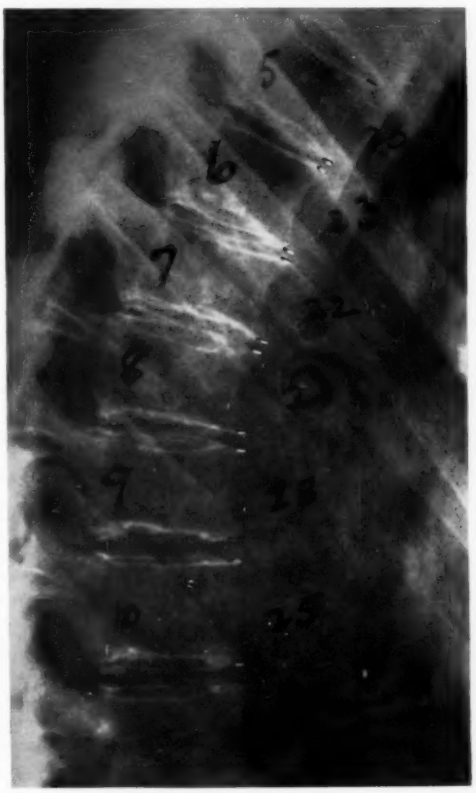
* References 1 and 2.

Many patients in the older age group will show evidence of degenerative arthritis. Synonyms for this type of arthritis are hypertrophic arthritis or osteoarthropathy, osteoarthritis, hypertrophic spondylitis, ankylosing spondylarthritis, spondylitis ossificans, and Bechterew's spondylitis (Fig. 2). These pathological changes are manifested by pains

Fig. 1.—Gradual wedging of vertebral bodies not exceeding 2 mm. and believed to represent healed osteochondritis rather than fracture.



in the back of varying incidence and degrees of severity and may be aggravated by unusual exercise. Roentgenologically, the features are increased kyphosis with anterior vertebral wedging involving a number of vertebrae, as compared with isolated involvement, as in fracture. Varying degrees of bony reaction develop, from lipping of the articulating margins to development of beaks and spurs

Fig. 2.—Degenerative arthritis with beaks and spurs projecting from the articulating margins and also showing minimal anterior wedging of vertebrae.

with intercentral bridging. There may be some evidence of osteoporosis (Fig. 3), but this is a difficult thing to estimate, because of varying technical factors. By this, we mean that a bone can be made to appear osteoporotic if one uses a large enough quantity of x-ray exposure. Presumably, it indicates absorption of calcium salts and makes the bones friable and prone to fracture.[3]

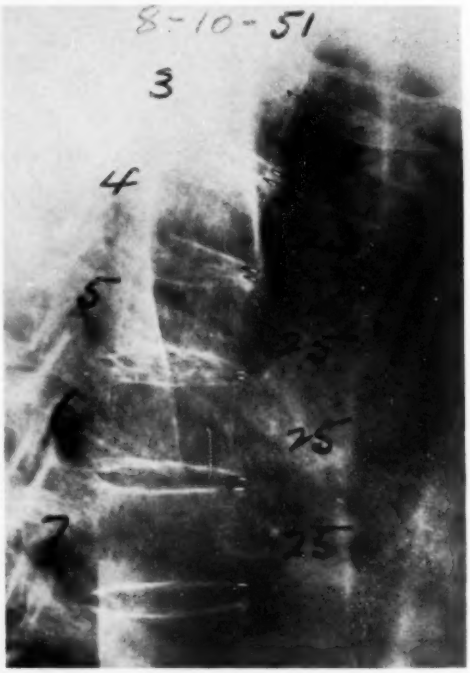


Fig. 3.—Demineralization or osteoporosis usually seen in older patients, showing thinning of the cortex and prominence of the trabecular pattern.

Fig. 4.—Biconcave deformities of vertebral endplates due to impressions of large nuclei pulposi, and not fractures.

Many spinal x-ray examinations will also show biconcave deformities due to pressure of large nuclei pulposi, but these may usually be regarded as developmental changes, and not as end-plate fractures (Fig. 4). The so-called Schmorl nodes (Fig. 5) will occasionally be seen, due to actual herniation of the nucleus through the vertebral plates. These may later calcify, but have little or no clinical significance.[4] There is a definite

Fig. 5.—Actual herniation of the nuclei pulposi through the end-plates (Schmorl's nodes). These often later calcify.

entity, described some years ago by Kummell, called spondylitis traumatica tarda, in which initial x-ray examinations show no macroscopic evidence of fracture but after some months progressive flattening of a vertebra may be demonstrated, believed due to the effect of weight bearing on the damaged vertebral segment.[5]

From these considerations it is clear that we must have initial films of our patients in order to know about the conditions we have enumerated and to determine the presence of any other evidence of fractures previously incurred, as from accidents, tetanus,[6] epileptic seizures,† or previous convulsive therapy. From the medicolegal standpoint, we cannot prove a fracture was not incurred during present therapy if we have no admission film to prove it. It is also advisable to have spine films on admission in order to be informed about such lesions as primary or metastatic malignant tumors. One hemangioma of a vertebra was seen in this series.

There are x-ray technical filming difficulties to be considered in analysis of this problem (Table 5, Part I). Frequently we have an uncooperative patient, and this occurrence will almost completely preclude radiographic procedures, as motion is the greatest enemy of detail in any photographic process. If the patient's cooperation is obtained, care must be taken to secure as true a lateral view with identical centering as possible, with use of the same tube-object distance, because a 36-in. film cannot be accurately compared with a 72-in. one. Even with optimal conditions satisfied in these respects, it is difficult to demonstrate clearly T 1, 2, and 3 without use of a laminagram. Usually we check for evidence of compression on the A. P. view, but this is not as reliable as the true lateral projection.

From the roentgenologic standpoint, the vertebral fractures we see are (1) compressed fractures of the centrum with characteristic wedging anteriorly, or (2) depressions of the vertebral end-plates, usually the superior ones caused by herniation of the nucleus pulposus, or (3) combinations of the two. Figure 6 shows an example of superior end-plate depression or fracture caused by pressure of the nucleus pulposus. We have experienced some difficulty in deciding what is to be labeled C. F., as the structural changes are often minimal. Some authors[8] have used a percentage of the anterior vertebral height, in millimeters, as the criterion, any compression in excess of 33% being considered a serious fracture. This usually will amount to

† References 6 and 7.

from 6 to 9 mm., as the thoracic vertebral anterior vertical measurements average from 20 to 28 mm. Such fractures as these are obvious on comparison films, but certainly vertebrae having slighter degrees of compression must also be included as fractures. Other authors ‡ have merely classified the fractures as mild, moderate, and severe. Cupping of the vertebral end-plates was regarded as "mild," moderate anterior compression as "moderate," and severe anterior compression as "severe." These general terms admit of considerable latitude in interpretation, and therefore variation in statistical findings. It seems to us that some more exact method of measurement should lead to greater uniformity of interpretation. We have arbitrarily considered a vertebra to be compressed if it measures at least 2 mm. or more less in anterior vertical height than on the control film. We chose 2 mm. as the minimal amount we could measure accurately on comparative films, and we feel that such a variation must represent some actual structural change. Differences of 1 mm. are considered insignificant and may be due to failure to place the guide marks at exactly the same places on the articular plates when measuring.

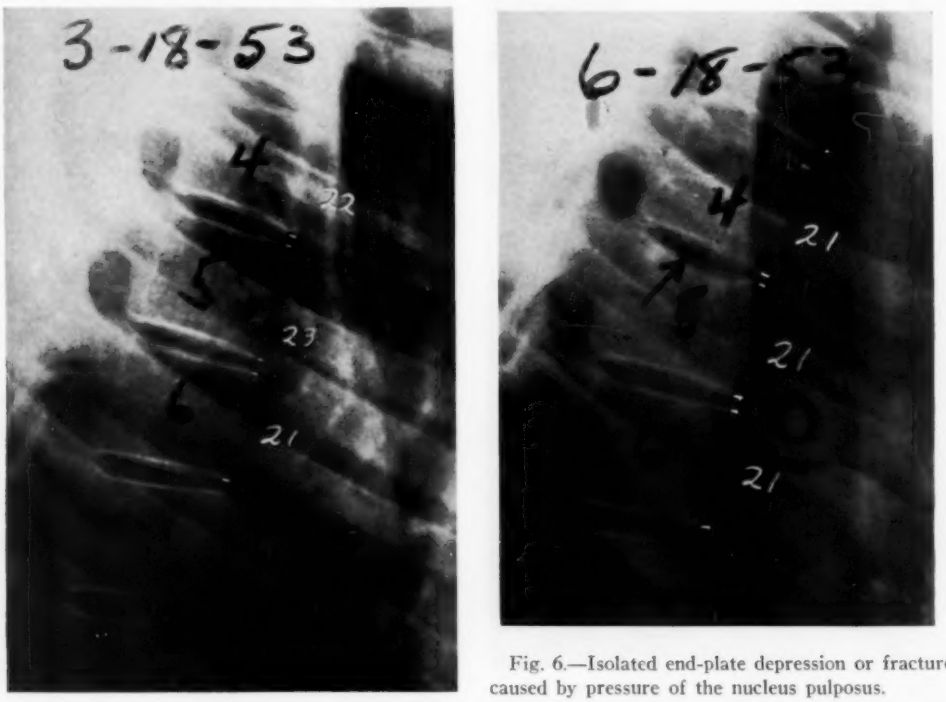


Fig. 6.—Isolated end-plate depression or fracture caused by pressure of the nucleus pulposus.

‡ References 9 and 10.

CLINICAL SURVEY

During the year Feb. 1, 1953, to Jan. 31, 1954, a total of 106 patients received electroconvulsive therapy (ECT) at Western Psychiatric Institute and Clinics (W. P. I.). Complete pre-ECT, post-therapy pain, and post-ECT x-ray data are available for 85 of these patients. Twenty male and 65 female patients, ranging in age from 16 to 73 years, received a total of 2472 treatments over a span of six years. The total number of treatments per patient ranges from 1 to 205, with an average of 29.1 treatments. Four ECT machines have been in use during this period: (1) Reiter CW 46J, (2) Reiter CW 47, (3) Offner, Type 736A, and (4) Pittsburgh Electroshock Unit.[11] The majority of the treatments were given with the Reiter

machines, and the glissando technique was used in well over 90% of the treatments given. Curare was used in selected cases. Routine indications included (1) x-ray evidence of moderate or advanced hypertrophic osteoarthropathy, (2) x-ray evidence of vertebral fracture during the course of ECT, and (3) clinical evidence of severe "jackknife" convulsive pattern. Only 13 of the 85 patients received curare. Only 2 of the 23 patients who sustained vertebral fracture during the series of treatments received curare. This gives some indication of the number of vertebral fractures sustained and unrecognized during the course of therapy. Treatments are given individually on a ward assigned for this purpose. The patient lies supine, arms at sides, on a padded wooden table. Hyperextension is encouraged by use of a small, firm pillow placed under the thoracic spine. Manual restraint is applied by four student nurses, holding the shoulders, forearms, hips and thighs. The pressure exerted is sufficient to favor hyperextension of the spine and to prevent gross lateral distortion of the extremities. One graduate nurse holds the electrodes in position, and a second supports the jaw with the tongue protector in place. Committed patients unable to cooperate for routine procedures receive treatment in a pack bed.

In this series of 85 patients receiving ECT, skeletal complications other than vertebral fractures include (1) unilateral temporomandibular jaw dislocation, (2) dislocation of the shoulder with history of recurrent dislocation prior to ECT, and (3) dislocation of the elbow with history of recurrent dislocation prior to ECT. In our experience, jaw dislocations are reduced spontaneously or manually with little difficulty if the diagnosis is made before the patient awakens from the treatment. When the dislocation is recognized after the patient awakens, thiopental (Pentothal) anesthesia is often required for reduction. In this connection, it is noteworthy that we have never seen a jaw dislocation occur when a Reiter machine was used. It is perhaps of interest that the patient who sustained the unilateral temporomandibular jaw dislocation noted above also had a vertebral fracture resulting from this first, and only, electroconvulsive treatment. Four months later, following his 46th insulin coma treatment, he complained of pain in the right shoulder and was found to have a fracture of the scapula. His characteristic pattern of response during second-stage coma included severe clonic spasms without any evidence of grand mal convulsions, spontaneous or induced. Approximately 500 patients have received ECT during the 10 years of its clinical use at W. P. I. Skeletal complications other than vertebral fracture during this period include (1) one fracture of the right femur, (2) one fracture of the sternum at the junction of the manubrium and the gladiolus, and (3) jaw dislocations. The fracture of the sternum was noted after one electroconvulsive treatment and 15 insulin coma treatments. It is probable that the fracture resulted from ECT, but responsibility is assigned with difficulty. In 1947 a fracture of the humerus occurred as a result of insulin coma with spontaneous grand mal convulsion. The evidence here suggests that insulin coma deserves as much attention as ECT when skeletal complications are considered. There also seems to be evidence inviting speculation about the possible significance of psychodynamic relationships. Would it perhaps be possible to predict "fracture proneness" on the basis of predominant psychodynamic patterns of behavior operating at the time of treatment? There is nothing from the roentgenologic standpoint that will permit us to predict the site of vertebral fracture or proneness to fracture in any given case. Holt [12] submitted 100 preshock spine films to an orthopedist—50 of them had postshock compression fractures; 50 had none. The orthopedist had "only chance success" in selecting the fracture-prone cases.

A summary of data relating to the incidence of vertebral fractures in this group of 85 patients is given in Table 1. It will be noted that the over-all incidence of such fractures is 27%. This figure is "after correction," as we have found in a critical analysis of our cases that accurate measurements

TABLE 1.—*Vertebral Compression Fractures* (Western Psychiatric Institute and Clinics)

	Total	Men	Women
Total no. of patients	85	20	65
Age range, yr.	16-73	16-68	20-73
C.F., no. of patients	23	4	19
Age range, yr.	20-62	39-62	20-57
% of total	27	20	29.2
Previous ECT, no. of patients	51	9	42
C.F. on admission	17	4	13
Add. path. after ECT	6	2	4
No C.F. on admission	34	5	29
C.F. after ECT	7	1	6
Pain, total no. of patients	12	1	11
With C.F.	6	1	5
Without C.F.	6	0	6
C.F. without pain	17	3	14

discovered this variation when evaluating our material and decided we would have to make more detailed measurements to determine the existence of compression and the degree of progression of such compression fracture. Before correction by this method our fracture incidence was 15.3% of 85 cases. After correction it rose to 27%. Others[13] have stated that incidence of fracture will vary with the observer. It therefore seems important in such an evaluation as this that actual vertebral measurements be made. We indicate what is meant in Figure 7. Marks

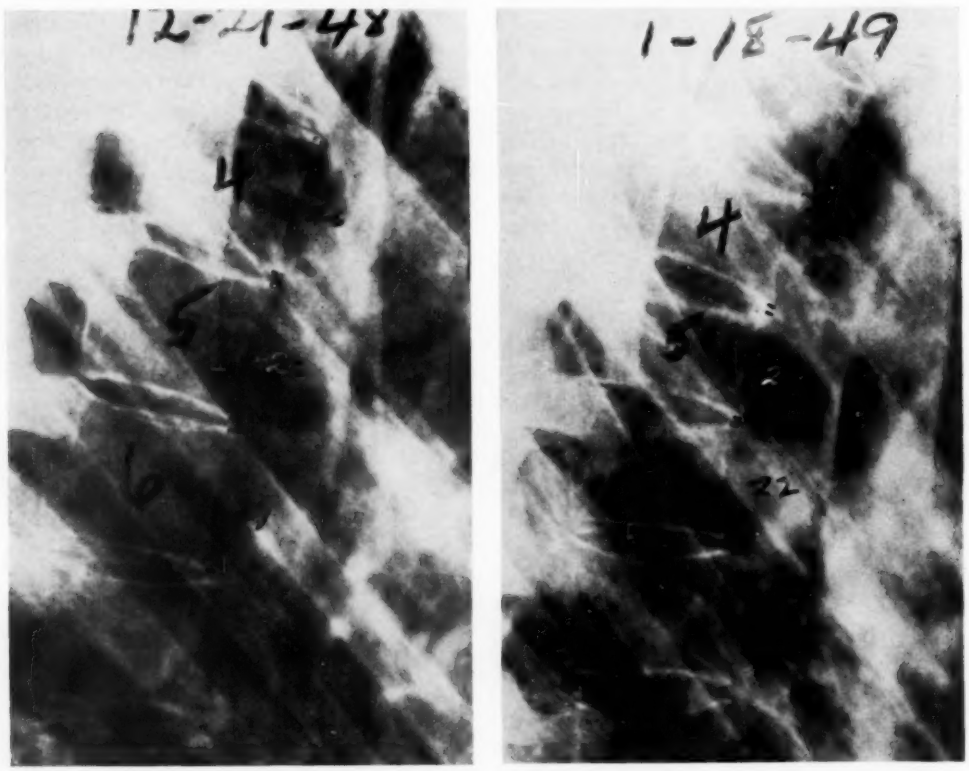


Fig. 7.—Marks have been made at the exact anterior edges of the vertebral plates so that accurate comparisons can be drawn. Note the 5 mm. compressions of T 5 and 6.

must be made, especially for comparative purposes. It is not sufficient merely to appraise comparative films with the eye. Definite measurements must be made. We have found that such a method may change the reported incidence as much as 11.7%. We are made at the exact anterior edges of the vertebral plates above and below, and the vertical height is marked in millimeters for subsequent comparison. This case was a corrected one, which previously was called negative, but in which compressions in excess of 4 mm. are demonstrated here. It is apparent that fracture incidence will vary considerably with the technique of x-ray examination and

TABLE 2.—*Vertebrae Involved in Compression Fractures*
(Western Psychiatric Institute and Clinics)

	Thoracic Vertebrae*									
Compression Fractures Diagnosed After ECT	3	4	5	6	7	8	9	10	11	12
23 Patients	o	x	x	o	x	x	x	o	..	..
46 Vertebrae involved	o	o	x	o	x	o	o	o	..	..
2 Vertebrae per pt.	..	o	o	o	o	o	o	..	..	..
100% Vertebrae T 3—10	..	o	o	o	o	o	o	..	..	..
91.3% Vertebrae T 4—9	..	o	o	o	o	o	o	..	..	..
52.2% Vertebrae T 5—7	..	..	o	..	o	o	o	..	..	..
	..	..	o	..	o	..	..	..	..	..
	..	..	o	..	o	..	..	..	..	..
	..	..	o	..	o	..	..	..	..	..
	2	6	9	5	10	6	6	2	..	..
Compression Fractures Diagnosed Prior to ECT	3	4	5	6	7	8	9	10	11	12
24 Patients	o	x	x	x	x	x	o	o	..	x
54 Vertebrae involved	..	x	x	x	x	o	o	..	..	x
2.3 Vertebrae per pt.	..	o	x	x	x	o	o	..	..	..
100% Vertebrae T 3—12	..	..	o	x	o	o	o	..	..	..
79.6% Vertebrae T 5—8	..	..	o	x	o	o	..	..	..	..
64.8% Vertebrae T 6—8	..	..	o	x	o	o	..	..	..	..
	..	..	o	o	o	o	..	..	..	..
	..	..	o	o	o	o	..	..	..	..
	..	..	..	o	o	o	..	..	..	..
	..	..	..	o	o	o	..	..	..	..
	..	..	..	o	o	o	..	..	..	..
	..	..	..	o	..	o	..	..	..	..
	1	3	8	12	11	12	4	1	..	2

* x indicates male patients; o, female patients.

the criteria used for diagnosis of fracture. Furthermore, it is important to make accurate sequential measurements to determine whether there is progression in C.F. Some cases show small degrees of increasing compression which are appreciable only on direct comparative measurements.

In Table 2 are shown the number of vertebrae fractured and the range of vertebrae these fractures cover. In the patients in whom no previous fractures had been demonstrated the range extended from T 3 to T 10. From T 4 to T 9, the incidence was 91.3%, while more than half the fractures (52.2%) occurred between T 5 and T 7. Of the fractures found in 24 patients on initial x-ray examination the range extended from T 3 to T 12, but the great majority of the fractures (79.6%) were between T 5 and T 8, while 64% involved T 6 to T 8. Thus,

TABLE 3.—*Vertebrae Most Frequently Involved in Compression Fractures*

	Cervical			Thoracic												Lumbar			Sources for Composite Data
	5	6	7	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	
Trauma	X	X	X	..	..	..	..	..	..	..	..	..	..	X	X	X	X	..	Refs. 10, 14, and 15
	X	X	X	..	..	..	..	..	..	..	..	..	..	X	X	X	X	..	
	X	X	X	..	..	..	..	..	..	..	..	..	..	X	X	X	X	..	
Epilepsy	..	..	..	..	..	X	X	X	X	X	X	X	X	X	X	X	X	X	Refs. 6, 7, and 16-18
	..	..	..	..	..	X	X	X	X	X	X	X	X	X	X	X	X	X	
	..	..	..	..	..	X	X	X	X	X	X	X	X	X	X	X	X	X	
Metrazol	..	..	..	..	..	X	X	X	X	X	X	X	..	..	..	..	..	..	Refs. 7, 15, 17,
	..	..	..	..	..	X	X	X	X	X	X	X	..	..	..	..	..	..	19-25, and 31
	..	..	..	..	..	X	X	X	X	X	X	X	..	..	..	..	..	..	
ECT	..	..	..	..	..	X	X	X	X	X	X	..	..	..	..	..	..	..	Refs. 7, 13, 16,
	..	..	..	..	..	X	X	X	X	X	X	..	..	..	..	..	..	..	26-30, and 32
	..	..	..	..	..	X	X	X	X	X	X	..	..	..	..	..	..	..	

it appears from our material, and this finding is in agreement with most other series, that the fractures are most frequent in convulsive therapy in the middle third of the thoracic spine, or from T 4 to T 8 (Table 3).

Clinical data relating to age, sex, previous ECT, vertebral fractures diagnosed prior to ECT at W. P. I., and subjective complaint of pain during the course of ECT are given in Table 1. With respect to age, the group consisted of 20 male patients, ranging from 16 to 68 years of age, and 65 women, ranging from 20 to 73 years. Breaking these down into age groups, there were 6 patients under 21 years, with two compression fractures, or 33%; 67 patients from 22 to 55 years, with 18 fractures, or 27%, and 12 patients over 55, who had 3 compression fractures among them, or 25%. While these numbers are small for purposes of comparison, age does not seem very significant as a factor predisposing to fracture. With respect to sex, 19 of the 65 women (29.2%) and 4 of the 20 men (20%) sustained vertebral fractures. As the over-all incidence was 27%, these figures suggest that sex is not a significant factor in the production of vertebral fractures. References to statistical data in the literature relating to factors of age and sex may be found in Part I. Fifty-one, or more than 50% of our patients, had previous ECT. Of these, 17 had x-ray evidence of compression fracture on admission, and during treatment six new fractures were sustained, or an incidence of 35%. Of the 34 patients with previous ECT and without demonstrable evidence of fracture on admission, 7, or 20%, incurred fractures. Of the 34 patients who had not had previous ECT, 10, or 29.4%, incurred vertebral fractures. The trend here substantiates in general the evidence[31] suggesting that patients who do not sustain vertebral fracture during an initial course of ECT are not as likely to develop fractures with subsequent treatment. These figures would also tend to support the work of Meschan, Scruggs, and associates,[32] who found that previous therapy will predispose to vertebral fracture only if associated with "anterior narrowness." The figures (Table 1) relating to subjective complaint of pain during a course of ECT indicate that 50% of the patients (12 of the total 85) who complained of pain were shown to have compression fractures. But these 6 with pain represent only 25% of the 23 with compression fracture. Thus, 75% of the patients with fractures did not complain of pain, and if we had x-rayed only those so complaining, we would have found only 6 of the 23 with fractures. This suggests that pain or its absence is not a reliable indicator of vertebral fracture in psychiatric patients.

SUMMARY

Admission x-ray examination of the thoracic spine is essential to determine the presence of previous trauma and various other pathologic changes. This is imperative also from the medicolegal standpoint and as a means of giving one a film for comparison following convulsive therapy.

Actual measurements of vertical heights of vertebrae in millimeters should be made in order to appraise accurately the existence of compression of at least 2 mm. It is not sufficient merely to make a visual estimation. Failure to make accurate comparative measurements may account for some of the wide variations in incidence of vertebral fractures in convulsive therapy reported. X-ray examination per se is not as important as critical film interpretation.

In agreement with other studies, our results show that vertebral fractures resulting from ECT are most frequent from T 4 to T 8.

In this series, of 85 patients, the factors of age and sex do not seem to be significantly related to incidence of vertebral fracture.

The evidence in this study suggests that the presence or absence of subjective pain is not a reliable criterion for diagnosis of vertebral fracture. Seventy-five per cent of our patients with fracture did not complain of pain.

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Behavior of Epileptic and Nonepileptic Patients with "Temporal Spikes"

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Recent advances in recording technique have reawakened interest in the interrelationship of electroencephalographically detectable cerebral activity and both normal and abnormal behavior. Much of this attention has centered about dysfunction of the temporal lobe and its subcortical connections in regard to disordered behavior. In particular, Heath and associates [13] have reported a specific electrophysiologic abnormality in these brain areas in schizophrenia. An interest in temporal lobe disorders has also been fostered by the study of psychical seizures, which have long been of clinical importance because of their similarity to psychotic states. Gibbs [7] and Hill [8] have emphasized the incidence of personality disorders in temporal lobe dysfunction, and Hill has called attention to the presence, in such patients, of "episodic behavior" other than epilepsy, i. e., acute catatonic states and impulsive emotionality.

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This paper represents our conclusions from a study by ourselves and Dr. Russell R. Monroe, Dr. Melvin Sabshin, and Miss Leona Bersadsky.

The aim of our study has been to investigate the behavior of a group of patients with known cerebral pathophysiologic changes, as indicated by an electroencephalographic abnormality, namely, temporal spiking. Study of such a group is one approach to the problem of the interrelation between behavior and central nervous system function. Such a study does not imply a simple parallelism of the two, nor does it attempt to establish any causal relationships. Particularly, it is not the intention of this paper to ascribe any specificity or unique role in total behavior to the temporal lobe. The specific localization of the electroencephalographic "focus" is of less importance than its indication of disturbed central nervous system physiology.

In a study of 56 patients with anterior temporal foci on the electroencephalogram, Hill [8] found 36% to exhibit "abnormal personality"; 36%, "psychopathic aggression"; 9%, "antisocial behavior"; 55%, "disturbed interpersonal relationship," and 59%, "neurotic symptoms." These findings are of definite interest to both clinician and research worker, but, unfortunately, it was not made clear just how extensive the psychiatric evaluation was or what diagnostic criteria were used. It is our purpose to investigate a similar group more exhaustively and more specifically in regard to personality traits and the kind and degree of clinical disturbance. In particular, we were interested in the relationship between overt psychosis and "temporal lobe" seizures, and in the extent to which psychologic disorder may be identified in patients with temporal

spikes who have no previous history of psychiatric treatment.

METHOD

A group of 42 patients was selected for study. Practical limitations compelled certain arbitrary considerations in the selection of the patient group. All patients, examined over a three-year period since the opening of our EEG station, who showed unilateral or bilateral temporal spike foci were chosen. In a few patients such foci were associated with abnormalities in other brain areas. The group included many patients who had received routine examinations while on the psychiatry or neurology services of a general hospital and also some patients who had been referred from other services for an electroencephalographic examination while being evaluated for suspected cerebral pathology. All children up to the age of 16 were excluded. Many patients with lesional brain disease were not available at the time of this study, so that the group does not fairly reflect the incidence of such disorder.

All 42 patients thus selected were then reexamined by repeat electroencephalography, including activation by hyperventilation and sleep, using monopolar techniques. Each patient was then seen by a psychiatrist for a detailed interview and mental status examination. When possible, members of the patient's family were interviewed as well. Those patients in whom there was no evidence of overt psychosis were seen by a second observer, who further explored areas of impaired function and, in particular, further evaluated any initial impression of "primary" schizophrenia, this diagnosis being based on the primary symptoms of autism and disturbances in thinking and affect, as described by Bleuler. The actual diagnosis of primary schizophrenia was made with caution but was considered to be of importance in evaluating the kind and degree of clinical disturbance. All final case protocols included a nosological diagnosis; a description of the character, that is, the established patterns of adaptation; a detailed record of the interview, and a summary of the chief symptoms, with particular attention to episodic phenomena. (Episodic phenomena included acute psychotic episodes; epilepsy, and disturbances of consciousness, affect, ideation, perception, and visceral function which appear suddenly and are self-limited. Many of these last-named disturbances appear in psychotics, or in epileptics as auras or seizures. They also are seen in persons without clinical epilepsy who have emotional disturbances. These phenomena will be called here "episodic symptoms" to differentiate them from epileptic symptoms.) Since many of the patients had been hospitalized on our psychiatric and neurologic wards or had attended the clinics of our services, additional detailed histories and recorded observations of ward behavior were available.

Each patient was given a complete neurologic examination, including a careful history of epileptic symptomatology. Special note was made of such disturbances as body-image distortions, aphasia or paraphasia, and dyscalculia. For those epileptic patients in whom there was no evidence of structural neurologic disease on examination or routine investigative procedures the diagnosis of "idiopathic" epilepsy was made. This does not, of course, imply the absence of possible structural defects in this group.

A selected number of patients from the group were evaluated independently by means of psychologic techniques without any prior knowledge of the psychiatric or neurologic findings. Twenty patients in the series were found to have no previous history of medical treatment for disordered behavior or extensive contact with any other "helping agency," such as "personal counseling," Alcoholics Anonymous, and chiropractic. The study of this subgroup of patients offered a unique opportunity to obtain data as to whether such persons are in any way disturbed in their behavior or psychologic functioning, despite an absence of behavior disorder as a sufficient complaint to bring them to psychiatric attention. It was thought that a careful examination of this group with psychologic measurement techniques and a comparison of the findings with those made during psychiatric interviews would be most helpful in the attempt to round out a picture of the interrelation of abnormal temporal lobe electrical activity and patterns of behavior.

Three techniques of investigation were employed which have been proved effective in the detection of psychologic disorder. Briefly, they are the Rorschach Test, a projective test of personality structure [2]; psychomotor measures of the time of initiating movements, speed in continuing movement, and movement dexterity, which have been shown by King [9] to parallel the degree of disordered behavior in schizophrenia, and the Tulane Test-Behavior Scale, which is a method of making systematic notation of the behavior exhibited during psychological testing. This technique has been found to be effective both diagnostically, as a way of indicating the degree of deviation of abnormal behavior, and as a method for systematically following alterations in behavior consequent upon therapy.*

RESULTS

Diagnosis

There was a high incidence of psychiatric disturbance in this group of 42 patients. For

* References 9, 13, and 14.

34 (81%) a diagnosis of schizophrenia was made, 24 of them showing secondary symptoms. Only six were said to have psychoneurotic or personality pattern disorders, and two were considered as emotionally unstable personalities (Table 1).

Thirty-one patients had clinical epilepsy, 70% of whom had "idiopathic" psychomotor seizures, occurring either alone or in combination with grand mal seizures. Of these patients with psychomotor epilepsy, 90% were schizophrenics, 60% showing secondary symptoms. Of the nine patients with no clinical seizures seven were schizophenric. However, all of these seven patients had acute overt psychotic reactions, in contrast to only 5 with such reactions in the remaining 33 patients (Table 1).

TABLE 1.—*Diagnosis and Incidence of Acute Psychosis*

	No. Patients	Diagnosis				
		Primary Schizophrenia	Secondary Schizophrenia	Emotional Instability	Psychoneurotic or Personality Pattern Disturbances	Acute Psychosis
No epileptic seizures	9	0	7	2	0	7
Hysterical seizures	2	2	0	0	0	0
Psychomotor seizures, "idiopathic"						
Complex seizures	8	4	3	0	1	1
Other seizures	4	0	3	0	1	1
Grand mal seizures, "idiopathic"	3	0	1	0	2	1
Psychomotor & grand mal seizures, "idiopathic"						
Complex seizures	6	1	5	0	0	1
Other seizures	3	1	1	0	1	1
Psychomotor & grand mal seizures, symptomatic	7	2	4	0	1	0
Total	42	10	24	2	6	12

PERSONALITY AND SYMPTOMATOLOGY

Twenty-nine of the 42 patients showed "episodic symptoms," such as sudden affective changes, sudden alterations in consciousness, e. g., déjà vu or fugue states, and hallucinations. As previously defined, this behavior was nonictal and did not occur during a psychotic period. Most of these symptoms, particularly the hallucinations, occurred in the group with complex psychomotor seizures. It is interesting that eight of the patients in this group showed auditory hallucinations and eight visual hallucinations which occurred apart from the ictal or overtly psychotic period (Table 2).

The nonepisodic symptoms were chiefly (23 patients) paranoid, hypochondriacal, or referential. Twenty-one of the group showed marked depressive symptoms, and 11, expressional (hysterical) symptoms. Eight showed persistent visceral symptoms, such as epigastric discomfort. Eleven were specifically noted to be hyperactive. The classical symptoms of schizophrenia, affective disturbances, disorganization and concretization of thought, and conscious ambivalence were very frequent. It is of interest that 8 of the 14 patients with "idiopathic" complex psychomotor seizures were considered to show "organic" changes on mental testing, e. g., paraphasia and dyscalculia, while only one other patient in the entire group without demonstrable brain pathology showed such symptoms.

Characterologically the group was distinguished by loosely organized and immature patterns of adaptation. For example, no clear-cut character description, such as "obsessive-compulsive," could be made. The common adaptive patterns were those of passivity, withdrawal, and dependency. Concurrent with these patterns, hypochondriasis and referential paranoid ideation were seen.

A few patients relied primarily on poorly organized hysterical behavior to achieve their passive dependent aims.

All the observers were struck by the severity of disturbance in these patients. This aspect is difficult to convey in statistical terms, and the following case history may serve to bring some of these features into focus.

CASE 1.—*Diagnosis of schizophrenia with "idiopathic" grand mal and psychomotor epilepsy.*

A 21-year-old woman was seen in the clinic for the treatment of seizures, present since the age of 13. Following an aura of a "lump in the throat," the patient had episodes of dizziness, headache, and inability to talk. During other seizures tearing off of her clothes or other more purposive behavior was shown. On many occasions she had "come to" in a strange part of town. In addition to this pattern, several typical grand mal seizures had been observed by the family. Except for the electroencephalogram, the results of all tests, including an air study, were normal.

When seen in the clinic, the patient reported poorly formed auditory hallucinations and vague referential material. She also complained of episodes of incapacitating acute anxiety and reported frequent episodes of "feeling strange." "Everything looks queer to me." There were many periods of depression, with crying spells and suicidal ideas. She was always untidily dressed, with uncombed, dirty hair, but at the same time she wore heavy make-up, costume jewelry, and flamboyant clothes and behaved in a coy, bizarrely seductive fashion. Her motor performance was awkward and manneristic. Her relationship with the physician was one of ambivalent infantile dependency and aloof suspicion. On mental status examination, her thought was found to be disorganized and fragmented, and there was marked impairment of the ability to abstract. Dyscalculia was present.

The past history revealed night terrors and nail biting throughout childhood and persisting to the present. As an adult, she had never held a job and had no friends or mature heterosexual relations, although there had been several adolescent sex experiences. At present she is closest to a man of 55, her neighbor, who brings her to the clinic. He apparently has no sexual contact with her. It is perhaps worth noting that many of her undressing episodes are in this neighbor's yard.

TABLE 2.—*"Episodic Symptoms" Occurring Nonictally and Not in Overt Psychotic Periods*

	No. Patients	Visceral	Auditory Hallucinations	Visual Hallucinations	Ideational	Fugue	Déjà vu	Depersonalization	Rage	Fear	Depression
No epileptic seizures	4	0	0	0	1	0	2	0	2	0	1
Hysterical seizures	1	1	0	0	0	0	0	0	0	0	1
Psychomotor seizures, "idiopathic"											
Complex seizures	7	0	3	4	1	1	3	1	1	2	1
Other seizures	4	1	0	0	1	2	2	0	1	0	0
Grand mal seizures, "idiopathic"	1	0	0	0	1	0	1	0	0	1	0
Psychomotor & grand mal seizures, "idiopathic"											
Complex seizures	4	1	2	3	0	3	3	3	1	2	0
Other seizures	2	0	0	0	1	0	1	2	1	0	0
Psychomotor & grand mal seizures, symptomatic	6	1	3	1	1	0	2	3	2	1	1
Total	29	4	8	8	6	6	14	9	8	6	4

The patient had no history of an acute psychotic state, and none was observed during a year's attendance in the clinic. All of the symptoms were improved somewhat on medication, but the patient became aware that she "felt better" after a major seizure or a prolonged fugue state and formed the habit of skipping medication to precipitate a seizure when she experienced mounting anxiety or depression.

RELATIONSHIP BETWEEN SEIZURES AND PSYCHOSIS

Of the nine patients with no clinical epilepsy, seven had acute psychotic attacks, five of which were primarily catatonic in symptomatology. Only five other patients in the entire group had acute psychotic reactions, and none showed hyperactive catatonic features. This is in marked contrast to the 17 patients with clinical epilepsy and a

diagnosis of secondary schizophrenia with overt hallucinations or structured delusional systems for many years, only one of whom presented a history of an acute psychotic episode. Two of the patients with complex psychomotor seizures did have acute psychotic episodes, which were identical in many respects to their seizures. These episodes were not qualitatively different in pattern from the seizure, were of brief duration, and were self-limited, raising the question as to whether these reactions did not represent outlasting seizure activity. Indeed, the catatonic reactions, while not unusual, if viewed in terms of "epileptic" symptomatology, showed many features in common with psychomotor seizures, as will be discussed below. The following case histories illustrate these points.

CASE 2.—*Diagnosis of catatonic schizophrenia.*

A 19-year-old youth had been in good health until two weeks before admission to the psychiatric service, when he complained of headache and began to talk in an unusual, explosive, and emotional manner. He became unpredictably assaultive. On one occasion he suddenly fled from his home and hid in some nearby bushes, from which he had to be removed forcibly. Upon admission to the hospital, he was alternately sluggish and hyperactive. He made sudden attacks on other patients and on his physician and was amnesic for these episodes. The patient frequently broke into prayer and just as abruptly stopped. His trunk and extremities often assumed inappropriate postures. Auditory hallucinations were almost constant, and there were frequent nightmares. He was treated with E. S. T. and showed improvement.

CASE 3.—*Acute psychotic episode resembling the patient's complex psychomotor seizures.*

A 19-year-old white woman had had seizures since the age of 7 years. In her seizures she frequently displayed stereotyped postures, such as lying across the bed in a seductive fashion, and automatisms, such as undressing. This type of seizure usually occurred in her father's presence. She also showed impulsive emotionality, such as rage directed at her mother. Other automatisms included repetitive emptying of her mother's purse and brushing her hair with her mother's toothbrush. There were fugue-like episodes of wandering, frequent depersonalizations, and déjà vu experiences. Grand mal seizures were rare but present.

For a period of 10 days she showed overtly psychotic activity, including visual and auditory hallucinations. There was persistent alteration of consciousness during this time, in which she did not recognize familiar people, and there was constant depersonalization. She made a direct murderous assault on her mother, apparently prompted by her hallucinations, after a long period of wandering around a strange town. During this time she attempted to seduce her father. This psychotic period was terminated at a time when the patient had a grand mal seizure.

RELATIONSHIP BETWEEN "TEMPORAL LOBE" SPIKE AND DISORDERED BEHAVIOR IN PATIENTS WITH NO PREVIOUS HISTORY OF PSYCHIATRIC COMPLAINT.

(*a*) *The Group as a Whole.*—The Rorschach Test was administered individually to each of the 20 patients having no history of previous psychiatric complaint. Test protocols were scored according to the Beck system.[2] In order to attach an approximate quantitative value to the records obtained, the following procedure was employed:

TABLE 3.—*Test Scores Obtained by the Temporal Group Without a Psychiatric History, and Normal Expected Values*

	Normal Average	Possible Range	Temporal Group
Rorschach	0	0-3	2.4
Psychomotor performance	50	1-100	28.4
Behavior ratings	40	0-40	33.4
RT variability	30.6	...	52.1

After all records had been scored in detail and their summary analyses written, the examiner was asked to sort the test productions of these 20 patients into three categories—those which were the least deviant from normal, those moderately deviant from normal, and those most deviant from normal. The least deviant group was then sorted again into records indistinguishable from the performance of a normal subject and those which contained some recognizable forms of deviation. Numerical values were then assigned to each of these four categories: 0, not distinguishable from normal; 1, least deviant from normal; 2, moderately deviant from normal; 3, most deviant from normal. The results of this relative scoring may be seen in Table 3. Since normal expectation is 0 and the possible range of scores lies between 0 and 3, the group average obtained of 2.4 indicates that

the group as a whole displays behavior disorder of considerable degree. No member of the group could be placed in the 0 category, all records being found to exhibit a departure from normal expectation. The detailed analyses of the productions of this group showed a heavy loading of signs usually associated with schizophrenia with marked anatomical and sexual preoccupation. As a group these records were found to be clearly more deviant from normal than those usually obtained from patients admitted to our outpatient psychiatric clinic.

The performance of this group on psychomotor tests which have been found to reflect the presence of behavior disorder [9] has been expressed in a single total score summing the performance on all subtests for each individual subject by first converting all to equivalent scores in a common distribution. The performance of the group, also shown in Table 3, may be seen clearly to exhibit retardation. The normal expectation for this (combined) measure is a score of 50, with a possible range of scores from 1 to 100, and σ of 14. The group average obtained of 28.4 thus falls at least 1.5σ below the mean. This level of performance is clearly below that usually obtained from patients admitted for treatment in our outpatient psychiatric clinic.

A systematic notation of the behavior exhibited by each patient while performing on projective and psychomotor tests has been made employing the Tulane Test-Behavior Scale.† These observations do not relate to the quality of performance on the tests themselves, but center on the patient's approach to the test and the behavior exhibited during the test session. A total score has been derived from the ratings made on each patient, and the average of this group is shown in Table 3 to be 33.4. Normal expectation for these ratings is a score of 40, with a possible range extending from 0 to 40. The temporal group average of 33.4 indicates impairment observed during test behavior of considerable magnitude, at least as great as that usually recorded among patients attending the psychiatric outpatient clinic.

One further indication of the status of this group is available in the form of a variability score obtained, i. e., the standard deviation of each subject's performance during 20 trials on one of the psychomotor tests, RT(L). As shown in Table 3, this value is increased for the temporal group (52.1) above the normal (30.6), indicating a trend toward greater irregularity of response in the temporal group. Increased variability in response is characteristic of performance on this test by patients with disordered behavior,[9] and thus this trend follows that found for the mean level of performance.

In summary, this group of 20 cases displays a tendency toward disordered behavior when considered on the basis of any of the three independent measurement techniques employed.

(*b*) *Subdivisions of the Group Made by Clinical Evaluations.*—Although the number of patients in this group is too small to permit confident subdivision and intercomparison, it is of interest to note what performance values are obtained when the group is subdivided as to the type of clinical seizure present. The scores on the psychologic tests given in Table 4 indicate these trends, and caution is urged in their interpretation in view of the small number of cases available.

It may be seen that on most bases of evaluation the group with no clinical epilepsy shows the least departure from normality, while the group with complex psychomotor seizures shows the greatest deviation. The grand mal group shows the next least deviation after the group with no seizures whatever, and the simple psychomotor seizure group exhibits somewhat greater disorder and is more like the most deviant group, with a complex psychomotor seizure pattern.

The results obtained on the special psychologic study of those patients in the series with no previous history of psychiatric dis-

† References 9, 13, and 14.

order sustain the notion that some degree of disordered behavior is associated with the presence of disturbed electrical foci in the temporal brain region, despite the fact that no one of the patients studied in this series of 20 cases had a history of problem behavior other than the seizure pattern. Although the methods of comparison employed here are more relative than absolute, it is clear that these patients are anything but a normal group as measured by three independent techniques for the registration of psychologic disorder.

The clinical evaluation of these 20 patients without previous psychiatric complaint confirmed that of the psychologists. More significant, perhaps, was the observation that these patients showed the same severity and pattern of disturbance as the 22 patients with psychiatric complaints, except for the presence of acute psychotic episodes.

Table 4.—*Test Scores Obtained by the Temporal Group Subdivided into Clinical Seizure Types*

	Normal Average	Possible Range	Temporal Group: No Epileptic Seizure	Temporal Group: Simple Psychomotor Seizure	Temporal Group: Complex Psychomotor Seizure	Temporal Group: Grand Mal Seizure
No. of patients	..	...	2	10	5	3
Rorschach	0	0-3	1.5	2.8	2.5	2.0
Psychomotor	50	1-100	48.5	29.8	—6.5	41.8
Behavior ratings	40	0-40	34.5	33.0	31.6	34.8
RT variability	30.6	...	35.2	59.1	81.1	33.0

COMMENT

Although in terms of the usual clinical categories the group investigated is heterogeneous, the patients show certain disturbances in common. The group showed disturbances in thinking and affect which have come to be associated with the schizophrenic process, and were so diagnosed in our evaluation. Perhaps as a corollary, almost all of the patients of this group showed infantile, poorly organized character structures. The majority of patients showed episodic behavior, which ranged in a continuum from brief depersonalization or mild visceral disturbances to transitory psychotic phenomena, such as hallucinations, to true epileptic phenomena and/or overt psychotic reactions. In some of the patients identical content was noted in these various episodic disturbances, raising the question as to whether there may be similar underlying physiologic mechanisms.

The episodic visceral disturbances may serve as the background for the high incidence of somatic complaints in these patients. Their subsequent elaboration into hypochondriacal ideation might then occur to attain dependency strivings or other needs arising from the patient's psychodynamic patterns. The presence of visceral complaints in epileptic patients whose seizures have been controlled has also been noted by Scott and Masland.[12] Those complaints which have a tendency to persist are termed "continuous auras" by these authors and seem to be dispelled by the occurrence of motor seizures. Scott and Masland have also noted the appearance of affective and intellectual disturbances as "continuous psychic auras." It is of interest that in their patients who showed clear electroencephalographic foci, temporal lobe spike discharges were the commonest.

In our series the patients with the most persistently severe psychiatric disturbance, on both clinical evaluation and psychologic testing, were those with psychomotor seizures, especially of the complex or psychical variety. This finding is in keeping with observations by Gibbs [7] and Gastaut [6] of the high incidence of psychiatric disturbance in such patients. In terms of the phenomena observed in complex psychomotor seizures this is not surprising. These seizures are characterized by alterations in the state of consciousness, depersonalization, déjà vu,

fugue and dream states, seemingly purposeful, but often bizarre, activity, stereotyped patterns of motor and speech behavior, visual and auditory hallucinations, affective outbursts, and forced ideation. It is clear that one or many of these symptoms can be seen in psychotic or hysterical states, and, indeed, there is often confusion in the differential diagnosis.

Hughlings Jackson pointed out the link between psychical seizures and dreams and speculated that insanity was a phenomenon more complex than, but qualitatively similar to, psychical seizures. Electrophysiologic support for this concept was furnished by Penfield and his collaborators, who demonstrated that electrical stimulation of the diseased temporal lobe would reproduce not only the specific seizure pattern of the individual patient, but also memories, dreams, hallucinations, and affective responses.

Another important development in the study of the interrelationship of psychoses and complex psychomotor seizures is the recent report of a subcortical electrophysiologic abnormality in psychotic states. Heath and co-workers [13] have reported abnormalities in the septal-hippocampal complex in schizophrenic patients. Other investigations by Bickford [3] and Delgado and associates [4] have also suggested a subcortical abnormality in psychoses. The finding of a high incidence of schizophrenic disturbance in our group is of interest in view of the finding by Heath and co-workers of "septal" spiking in the subcorticograms of schizophrenics. The septal area-fornix system has been shown to be one of several subcortical structures functionally connected with the temporal pole,[10] thus raising the question whether, in many of our patients, the temporal spikes are a reflection of subcortical abnormality.

When specifically compared with epileptic phenomena, the behavior of the five catatonic patients in our series, while not atypical of that usually observed on psychiatric wards, showed many similarities to the behavior often observed in psychomotor seizures—for example, hyperactivity; stereotyped, almost automatic, motor and speech patterns; affective outbursts, and even incontinence of urine (Table 5). In this regard may be mentioned Hill's observation of frequent electroencephalographic abnormalities in catatonics, this abnormality primarily taking the form of bilateral spikes, occurring in groups, and fast spikes and waves. It is also of interest that Hill and his associates have found that the paroxysmal electroencephalographic activity tends to disappear during periods of remission from the catatonic reaction. These workers also note that the seizure threshold, as determined by the combined photopentylenetetrazol (photo-Metrazol) technique, becomes lower as the catatonic patient recovers.

TABLE 5.—*Episodic Phenomena Occurring During Idiopathic Psychomotor Seizures and During Acute Catatonic Reactions*

	No. Patients	Visceral	Auditory Hallucinations	Visual Hallucinations	Ideational	Rage	Fear	Depression
Acute catatonic reactions.....	5	2	3	2	3	5	5	4
Complex psychomotor seizures.....	14	8	2	6	4	3	6	0

The presence of seizures seems to correlate negatively in our group with the presence of acute psychotic reactions, especially those of the catatonic type. This type of psychosis, which is a sudden qualitative alteration in behavior, most frequently with no previous counterpart in the patient's history, differs from the brief psychotic reactions seen in a few patients with complex psychomotor seizures in whom the psychotic reactions seem to represent outlasting seizure activity.

The clinical observation of the apparent reciprocal relation between seizures and psychosis has been noted for some time and

was, of course, the empirical basis for convulsive therapy of psychoses. Since that time, however, it has been evident that epilepsy and schizophrenia are not mutually exclusive. This, too, is clear in our group, in which many of the epileptics had long histories of psychotic symptomatology. However, the rarity of acute catatonic reactions in the epileptic patient is striking and may be of further significance. This cannot be adequately explained by our data, and perhaps no hypothesis can be made until the adaptive function of the seizure in physiologic and psychologic terms is further studied.[1]

The clinical implication from this study that there is a continuity of episodic phenomena suggests the assumption of a similar physiologic continuity and should lead to a study of such phenomena from the psychodynamic point of view. Of these phenomena, the most accessible to study are those of a complex ideational nature. Recently Ostow [11] and Epstein and Ervin [5] have used motivational interpretation to study the content of complex psychomotor seizures. These studies have pointed out that there is a clear link not only with the psychoses but also with the normal phenomena of dreams. It is felt that the psychodynamic study of patients showing such episodic phenomena, which can be concurrently investigated by physiologic techniques, will help to elucidate the mechanisms not only of disordered, but also of normal, behavior.

SUMMARY

Forty-two patients with an electroencephalographic finding of "temporal spikes" were studied by psychiatric and neurologic examinations.

The total group showed a high incidence of psychiatric disturbance. For 81% of the patients a diagnosis of schizophrenia was made. The group with the most marked persistent degree of disturbance, both psychologically and psychiatrically, is that with complex psychomotor seizures.

A special study of 20 patients of this series with no previous history of psychiatric disorder by means of psychologic testing techniques indicates that such patients are clearly impaired in psychologic functioning, as compared with normal subjects. On psychiatric evaluation, they are no less impaired than the other 22 patients with a complaint of psychiatric disorder.

The most frequent personality feature of the patients is the absence of a stable character structure. There is a high incidence of episodic disturbances of a visceral, perceptual, affective, or ideational nature. The type of episodic disturbance is varied, including nonictal, ictal, and grossly psychotic phenomena, suggesting that there is a similar associated physiologic mechanism in what are usually considered qualitatively different disorders.

It is noted that the presence of clinical epilepsy in this group tends to exclude the appearance of acute catatonic psychoses, even in otherwise overtly and chronically psychotic patients.

The importance of such behavioral studies in persons with altered central nervous system function for the further understanding of normal behavior is emphasized.

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The Syndrome of Increased Intracranial Pressure Without Localizing Signs

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A neurological service is often confronted by a patient who has increased intracranial pressure without any localizing abnormality evident on neurological examination. A common tendency is to suspect that such a patient has either "a midline obstructive lesion" or the syndrome that has been called "serous meningitis," "cerebral pseudotumor," or "meningeal hydrops." In our experience, however, a lateralized mass was frequently found despite the absence of focal neurological signs.

In view of this disparity, it was decided to make a systematic study of the problem.

METHOD

A survey was made of the operating room records at the Neurological Institute of New York from January, 1945, to September, 1953. The case histories of all patients who underwent ventriculography and/or craniotomy were reviewed. Excluded from the study were (1) infants who were under the age of one year (congenital hydrocephalus eliminated for the most part); (2) patients on whom operations had been performed for reasons other than possible intracranial mass lesions, and (3) patients who had acute head injuries.

It was also necessary to exclude a few private patients whose case records were restricted from use in research and a few patients whose case records were not traceable. Data were collected on 2000 patients who underwent ventriculography and/or craniotomy for a possible intracranial mass lesion.

The records of the patients who had increased intracranial pressure without localizing signs were selected for further study. The criteria for increased intracranial pressure were either papilledema or a cerebrospinal fluid pressure greater than 250 mm. of water. The phrase "no localizing signs" requires amplification. In evaluation of the presence or absence of focal signs, the following abnormalities were not considered to be localizing: impaired consciousness, lateral rectus weakness, diminished visual acuity with papilledema when not accompanied by localizing abnormalities of the visual fields, "nystagmoid" movements, and minimal unsteadiness of gait or minimal incoordination of the extremities if equal in degree on the two sides. Other focal neurological signs were regarded as having localizing value, even when the abnormality was described as "slight" in degree or when the deductions of localization from these signs were proved to be incorrect. If, however, one examiner reported a given sign as "doubtful" or "equivocal," this abnormality was not considered to be of localizing value unless corroborated by other examiners. When several observers disagreed about the presence or absence of a localizing abnormality, the case was considered to have a localizing sign whenever more than one of the examiners considered the abnormality to be beyond the "equivocal" stage.

A biopsy with histological confirmation was not obtained in every case. Nevertheless, these unconfirmed cases were included because the location of the mass seemed of greater importance than its pathologic type for purposes of this study.

The cases were grouped, according to, final diagnoses, into the following categories:

1. "Serous meningitis"
2. Midline obstructive lesions
3. Lateralized mass lesions
4. Miscellaneous

The frequencies of the various diagnostic categories were compared and correlations were drawn between the final diagnoses and the clinical or laboratory data, to be described below.

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RESULTS

A. Incidence.—Among the 2000 patients who had ventriculography and/or craniotomy for a possible intracranial mass lesion, there were 238 with increased intracranial pressure without localizing signs. Patients with this clinical problem appeared with an average frequency of approximately 25 a year at this 200-bed neurological hospital.

B. Final Diagnoses.—1. "Serous Meningitis": This diagnosis was made in 27 patients, or in 11% of the 238. The usual clinical criteria were used in making the diagnosis; namely, signs of increased intracranial pressure in previously healthy persons, absence of localizing neurological signs, a normal cerebrospinal fluid except for increased pressure, and a normal ventricular system. Following the original study of the 27 patients, there developed neither signs of neurological deterioration nor evidences of a focal lesion during the subsequent course. This observation period was two years or more in 17 cases, six months to two years in 5 cases, and two to six months in the remaining 5 cases.

2. Midline Obstructive Lesions: Sixty-two patients of the 238 (26%) were found to have a midline obstructive lesion as the basis of their intracranial hypertension without focal signs. The majority of these patients (36) had lesions in the third ventricle or at its outlet. A variety of intraventricular neoplasmas was found: glioma, eight cases; colloid cyst, six cases; pinealoma, two cases; craniopharyngioma, one case; tumor, histological type not verified, seven cases. There were 10 patients with aqueduct obstruction in whom no definitive diagnosis was made. Two children who had suprasellar masses in the absence of localizing signs were grouped with those who had lesions of the third ventricle.

The remaining 26 patients with midline obstruction had lesions at the level of the fourth ventricle. There were 17 with neoplasms in the fourth ventricle, 2 with nonneoplastic block of the outlets, and 7 with space-occupying masses within the pons or medulla.

3. Lateralized Mass Lesions: Forty-nine per cent of patients with increased pressure of clinically unlocalized cause proved to have lateralized masses (117 cases). Ninety-nine of these patients had lesions with a supratentorial position, but there were 18 infratentorial masses in one or the other cerebellar hemisphere. The 99 supratentorial lateral lesions comprised 56 intracerebral neoplasms, 20 extracerebral neoplasms, and 23 nonneoplastic masses. The histological types of these lesions are given in Table 1. It is noteworthy that the three most frequent diagnosis in this category were astrocytoma, meningioma, and subdural hematoma.

TABLE 1.—*Lateral Cerebral Masses: Histological Types*

Histological Type	No. of Cases
Astrocytoma	18
Glioblastoma	11
Oligodendroglioma	5
Other gliomas (including mixed)	7
Metastatic carcinoma	7
Meningioma	17
Hematoma, subdural	16
Hematoma, intracerebral	2
Abscess	4
Other masses (teratoma, sarcoma, "cyst"; masses not examined histologically)	12
Total	99

Of these cerebral hemisphere masses, the majority affected the nondominant hemisphere. There were 51 right-sided, 34 left-sided, and 14 bilateral masses. There were only six left-handed patients, three of whom had a lesion affecting the right hemisphere, two the left hemisphere, and one both hemispheres.

The 99 lateral masses were all clinically "silent." However, only 32 of them were confined to the expected "silent," nondominant frontal or temporal lobe.

4. Miscellaneous Lesions: This category includes 32, or 14%, of the 238 patients without focal signs. These patients could not be considered to belong to any of the previous three categories. A definitive diagnosis was established for only 8 of these 32 pa-

tients. The diagnoses were malignant hypertension, two patients; hypoparathyroidism, one; tuberculous meningitis, one; cysticercous meningitis, two; B. subtilis meningitis, one, and meningeal lymphosarcomatosis, one. It is to be emphasized that the diagnosis was not evident until ventriculography had been performed for suspected intracranial mass lesion.

Eight of the 32 patients were infants over the age of one year in whom the criteria for a diagnosis of communicating hydrocephalus were fulfilled. There remained 16 patients for whom no definitive diagnosis was made. Ventriculography revealed no evidence of tumor or of ventricular obstruction. The diagnosis of "serous meningitis" was not tenable because of an abnormality of the ventricular system or because of marked abnormality in the cerebrospinal fluid.

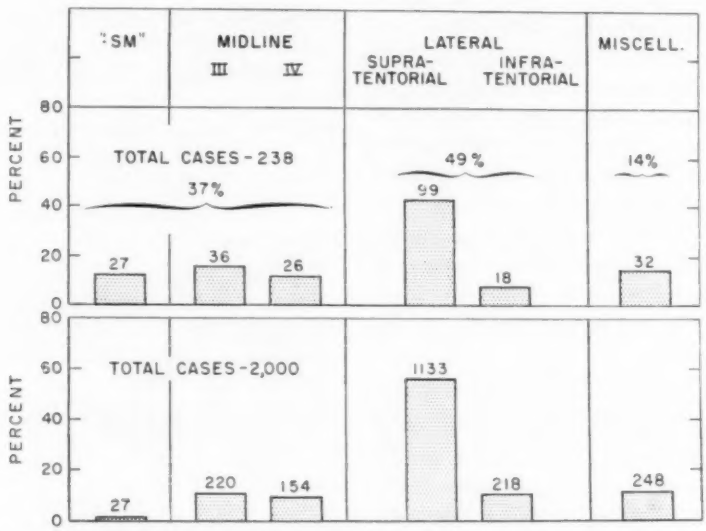

Fig. 1.—Upper: Final diagnoses in 238 patients with increased intracranial pressure but no localizing signs. Lower: The entire series of 2000 patients. *"SM"* indicates "serous meningitis."

C. Comparative Frequency.—The incidence of the final diagnoses in the 238 patients with increased intracranial pressure without localizing signs may be appreciated from a survey of the data summarized in the upper half of Figure 1. Forty-nine per cent of these patients proved to have a laterally placed mass lesion. Thirty-seven per cent had either "serous meningitis" or a midline obstructive lesion. In 14% of the patients, a definitive diagnosis was not possible, or, in a few instances, the final diagnosis did not allow the patient to be classified in any of the preceding categories. If the 32 cases (14%) in the miscellaneous category are set aside, one can compare directly the incidence of lateralized mass lesions versus incidence of "serous meningitis" and midline lesions. There are, then, 206 patients for whom the diagnosis proved to be one of the following:

	Patients	%	
"Serous meningitis"	27	13	43%
Midline obstructive lesion	62	30	
Supratentorial lateral mass	99	48	57%
Infratentorial lateral mass	18	9	

In the lower half of Figure 1 is presented an analysis of the final diagnoses in the total 2000 patients.

What proportion of the total patients in each diagnostic category presented with the syndrome of increased intracranial pressure in the absence of localizing neurological

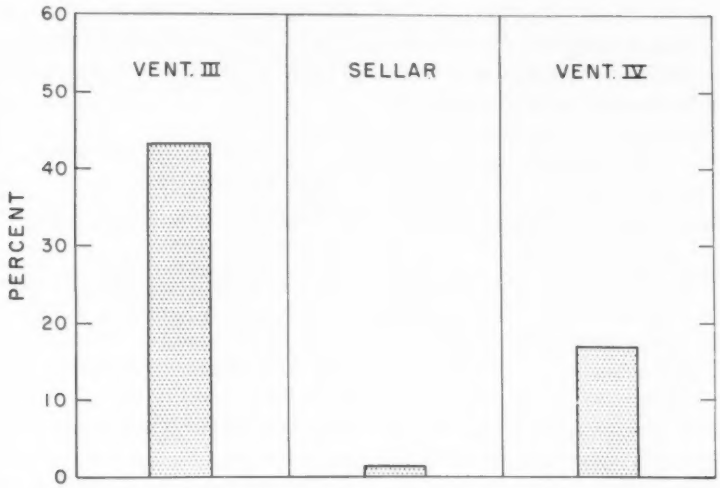

Fig. 2.—Percentages of the total cases with midline lesions who presented with increased intracranial pressure but no localizing signs.

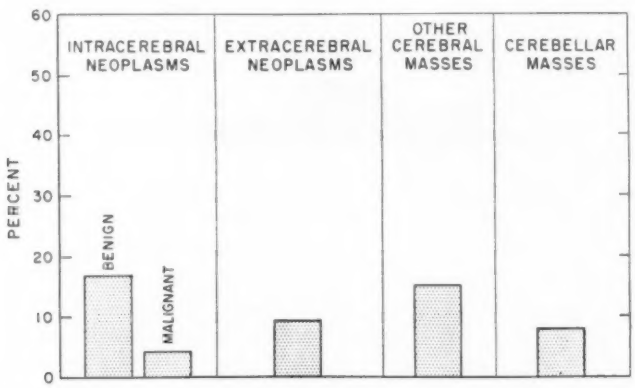

Fig. 3.—Percentages of the total cases with lateral masses who presented with increased intracranial pressure but no localizing signs.

signs? An analysis of the cases which had midline lesions is presented in Figure 2. Of 77 patients who had lesions in the third ventricle or at its outlet, 44% presented with signs of intracranial pressure only. By contrast, only 2 of the 143 patients who had lesions in or around the sella turcica presented in that fashion.* Twenty-six of the 154 patients (17%) with midline lesions obstructing the fourth ventricle presented with intracranial pressure without localizing signs. Of all patients with midline lesions, 17% presented with increased intracranial pressure alone.

A similar comparison for those patients who had laterally placed mass lesions is given in Figure 3. A note of explanation regarding the terminology "benign" or "malignant" intracerebral neoplasms is necessary. The designation "malignant" has been applied only to the glioblastomas, metastatic carci-

* The third ventricle lesions and the sellar lesions were differentiated in Figure 2 because of the marked disparity in the incidence of patients without focal signs. However, these two categories were grouped together in Figure 1.

nomas, and sarcomas. All other intracerebral tumors have been labeled "benign" for the purposes of this illustration. The total number of cases in each of the categories of lateral masses, and the proportion of each that presented with increased pressure but no localizing signs, are given in Table 2. Of 1351 cases with lateral mass lesions, 117 (9%) had only intracranial hypertension.

D. Clinical Variables.—1. Age: The age distribution of the patients in the three major categories ("serous meningitis," midline lesions, lateralized masses) is presented in Figure 4. It appears that with increasing age there is an increasing likelihood that the individual patient will prove to have a lateralized mass lesion.

TABLE 2.—*Lateral Masses: Proportion of Cases in Each Diagnostic Category with Increased Intracranial Pressure (IIP) and No Localizing Signs*

Lateral Masses	Total	IIP Non-localizing	Percentage
Intracerebral neoplasms			
"Benign"	207	35	17
"Malignant"	544	21	4
Extracerebral neoplasms	227	20	9
Non-neoplastic cerebral masses	155	23	15
Posterior fossa, lateral masses	218	18	8
Totals	1,351	117	9

2. Papilledema: Patients were considered to have increased intracranial pressure if they had either papilledema or a spinal fluid pressure greater than 250 mm. of water. Of the 206 patients with increased pressure and

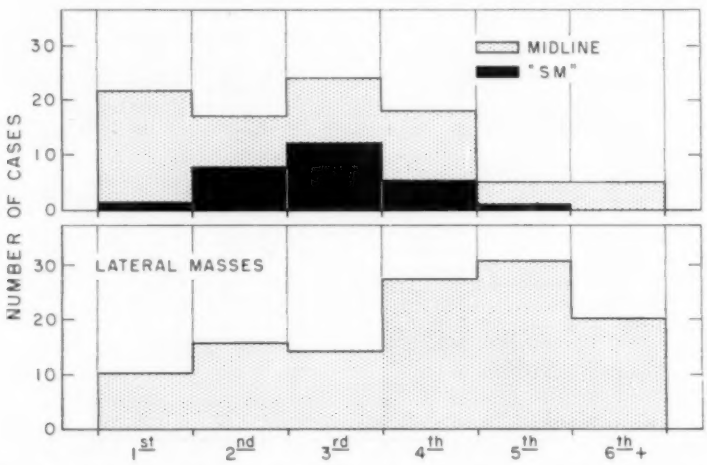

Fig. 4.—Age distribution, by decades, of 205 patients with increased intracranial pressure but no localizing signs.

TABLE 3.—*Comparison of the Total 206 Cases Having Increased Intracranial Pressure (IIP) with the 179 Cases Having Definite Papilledema*

Final Diagnoses	IIP With or Without Papilledema		IIP With Papilledema	
	No.	Percentage	No.	Percentage
"Serous meningitis"	27	13	26	15
Midline				
III ventricle	36	17	27	15
IV ventricle	26	13	26	15
Lateral				
Supratentorial	99	48	83	46
Infratentorial	18	9	17	9
Totals	206	100	179	100

no localizing signs (excluding the miscellaneous group), 179 had definite papilledema. The frequencies of the diagnostic categories can be seen in Table 3, in which the group of patients who had frank papilledema is compared with the total number studied. There is little difference between the two groups with respect to the incidence of each final diagnosis.

3. Equivocal Focal Signs: An effort was made to determine whether the inclusion of patients who had equivocal focal signs biased the results in favor of any of the diagnostic categories. The exclusion of all patients with equivocal localizing signs from the total group of 206 patients left 156, whose final diagnoses were as follows: "serous meningitis," 15%; midline obstruction at the third ventricle, 18%; midline obstruction at the fourth ventricle, 10%; lateral supratentorial mass, 49%; lateral infratentorial mass, 7%. There is, then, little change in the relative frequencies of the groups. Fifteen per cent of the patients still have "serous meningitis"; 28% have midline obstruction, and 56% have a laterally placed mass lesion.

4. Mental Status: The clinical material included patients whose mental status was altered to such a degree that the neurological examination was necessarily incomplete. This inclusion did not bias the results, since an analysis of the group of patients with normal mental status indicated that the relative frequency of each diagnostic category approximated that of the total series. Among 120 patients with normal mental status, the incidence of "serous meningitis" was 20%, of midline obstruction 28%, and of lateral masses 52%. Among 86 patients with mental abnormality, the incidence of "serous meningitis" was 3%, of midline lesions 33%, and of lateral masses 64%.

E. Skull X-Rays and Electroencephalograms.—Plain roentgenograms of the skull were of considerable help in differential diagnosis. Results of x-ray examination were recorded in the charts of 194 of the 206 patients. Conclusive focal radiological signs (pineal displacement, pathologic calcification, hyperostosis, or focal bony erosion) were found in 43 patients, or 22% of the 194. Thirty-three per cent of the patients with supratentorial lateral masses had one or more of these focal radiological signs. It is, however, important to note that 15 patients with increased intracranial pressure due to a cerebral hemispheral mass had no displacement of the pineal gland. In four of these cases there was a bilateral lesion.

In assessing the value of plain skull films, one may consider the results "helpful," "indeterminate," or "misleading." A "helpful" radiographic report was considered to be one that indicated a focal pathologic calcification or bony alteration, displacement of the calcified pineal, or a midline pineal gland in the presence of a nonlateralized lesion. The "indeterminate" roentgenograms were those that had no focal radiological signs and no calcified pineal gland. The "misleading" roentgenograms were those that had a midline calcified pineal gland, even though there proved to be a lateralized cerebral mass. With the use of these description terms, it was found that, of the 194 patients, the plain skull films were "helpful" in 60 patients, "indeterminate" in 119 patients, and "misleading" in 15 patients.

Results of electroencephalography were available for 144 of the 206 patients. These results were grouped according to whether the electroencephalogram was lateralizing or nonlateralizing, and whether this differentiation was correct or incorrect with respect to the final diagnosis. These results are listed in Table 4 under the headings of "lateralizing, correct and incorrect" and "nonlateralizing, correct and incorrect." The electroencephalogram was found to be "correct" in 97 instances (67%) and "incorrect" in 47 instances (33%).

Finally, there were those cases in which there was increased intracranial pressure without localizing signs, and in which both the electroencephalogram and the skull x-rays were interpreted as "nonlateralizing." There were 77 patients in this category, 66 of whom had frank papilledema. The final

TABLE 4.—*Results of Electroencephalography in 144 Patients*

Final Diagnoses	"Lateralizing"		"Nonlateralizing"	
	Correct	Incorrect	Correct	Incorrect
"Serous meningitis"	..	2	21	..
Midline				
III ventricle	..	5	14	..
IV ventricle	..	3	14	..
Lateral				
Supratentorial	39	1	..	34
Infratentorial	..	2	9	..
Totals	39	13	58	34

TABLE 5.—*Final Diagnoses in Cases of Increased Intracranial Pressure (IIP), No Focal Signs, Nonlateralized EEG, Nonlateralized X-Ray*

Final Diagnoses	IIP With or Without Papilledema		IIP With Papilledema	
	No.	Percentage	No.	Percentage
"Serous meningitis"	21	27	20	30
Midline				
III ventricle	12	16	8	12
IV ventricle	12	16	12	18
Lateral				
Supratentorial	24	31	18	27
Infratentorial	8	10	8	12
Totals	77	100	66	99

diagnoses in each of these groups are given in Table 5. It can be seen that of those patients in whom there was no clinical or laboratory evidence of a lateralized lesion prior to ventriculography, approximately 40% proved to have a laterally placed mass.

COMMENT

Our interest in this problem was aroused by the opportunity to follow a number of patients who presented only with headaches and papilledema in the absence of reliable localizing signs on clinical examination. A majority of the observers in these cases favored a preoperative diagnosis of "serous meningitis" or "midline obstructive lesion." When in several consecutive cases with this clinical syndrome ventriculography revealed large mass lesions in one or the other cerebral hemisphere, it was proposed to investigate the results of diagnostic studies in a large group of patients with the same problem. It was found that the syndrome of increased intracranial pressure without localizing signs was more frequently produced by lateralized mass lesions than by "serous meningitis" or "midline obstruction."

When focal signs (other than the false signs associated with increased intracranial pressure) were described as "slight, but definite," they were considered to be sufficient for clinical localization, even though that localization might be proved to be incorrect eventually. "Questionable" or "equivocal" signs were not accredited with localizing value unless corroborated by another observer. The exclusion of all patients with equivocal localizing signs did not materially alter the relative frequency of the final diagnoses. Fifty-six per cent of the cases still proved to have a laterally placed mass.

Kelly,[1] in 1951, presented data for comparison in his paper on colloid cysts of the third ventricle. He was able to collect 361 cases with intracranial "tumours" from the records of the National Hospital in London.

Twenty-one of these patients presented the syndrome of headaches, papilledema, and no localizing signs on examination. Of these, 9 proved to have laterally placed neoplasms, 10 had midline lesions (7 colloid cysts), and 2 were described as having "no tumour, probably sinus thrombosis." It is not certain that Kelly's figures are directly comparable with the data presented here, since it is not clear that he included all cases of non-neoplastic masses. His inclusion of cases of "no tumour, probably sinus thrombosis" among 361 cases of "tumour" is confusing. It seems, however, that there was a slight preponderance of the nonlateralized lesions over the lateralized masses.

These studies leave unanswered a crucial problem in the physiology of the nervous system. How can a mass lesion large enough to cause signs of increased intracranial pressure be present in a cerebral hemisphere without giving evidence of focal disturbance of cerebral function?

SUMMARY

1. In our experience, the syndrome of increased intracranial pressure without localizing signs was more frequently produced by lateralized mass lesions—gliomas, meningiomas, subdural hematomas—than by "serous meningitis" or "midline obstruction."

2. Plain skull films and electroencephalograms were of some assistance in differential diagnosis. With their aid, the clinician could be correct in the majority of cases when deciding the question of a lateralized versus a nonlateralized lesion. However, these laboratory aids were often indeterminate or misleading.

3. There was still a sizable number of patients in whom all clinical and laboratory evidence seemed to favor a diagnosis of "serous meningitis" or "midline obstruction" but who proved to have a laterally placed mass on ventriculography.

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The Electroencephalogram in Arteriovenous Anomalies of the Brain

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There are only a few reports in the literature on electroencephalographic findings in cases of arteriovenous anomalies of the brain, and most such reports are based on relatively small series or isolated cases. The present study is only part of a broader review, to appear in consecutive publications, of the clinical, radiologic, and surgical aspects of 51 cases of cerebral angioma seen at the Mayo Clinic between 1930 and 1954. In this study an attempt is made to consider the value of the electroencephalogram as a preliminary test and screening procedure in the diagnostic evaluation of arteriovenous anomalies. The degree and type of electroencephalographic abnormalities are considered in relation to type, extent, and location of the underlying lesion and are correlated with the duration and kind of certain outstanding clinical features.

MATERIAL AND METHODS

For this study all electroencephalographically recorded cases of arteriovenous malformation of the brain registered at the Mayo Clinic between 1948 and 1954 were reviewed. The material consists of 26 routine electroencephalographic recordings and two pentylenetetrazol (Metrazol) activation studies, recorded from 18 patients. All cases were verified by angiography, surgery, or necropsy. In two patients cranial or neck arteries had been ligated 14 and 6 months, respectively, prior to the electroencephalographic recording. In two other patients cranial operations had been carried out 20 and 2 years, respectively, prior to the electroencephalographic recording. Postoperative recordings were available on six patients.

The recordings were made with an eight-channel Grass electroencephalograph. Fourteen electrodes were used, consisting of five pairs of equally spaced, parasagittally placed electrodes, beginning at the inion and 1½ in. from the midline, one pair of electrodes in the temporal regions, and one pair of electrodes on the ears. Both scalp-to-scalp and scalp-to-ear linkages were used. Photic stimulation was carried out by using the stimulator described by Bickford and Moffet[1] (flash duration 50μsec.; intensity 250,000 f-c.). The routine recording was followed by a three-minute period of overbreathing in all except one patient and by photic stimulation in all except two.

RESULTS

In classifying the findings, the 18 cases were divided into five groups, depending on degree of electroencephalographic abnormality and its value in localizing the lesion (Table 1). In Table 2 the individual cases are listed within their particular groups. The duration of symptoms before the electroencephalogram, the age of onset, the findings on examination, the type of seizures, the location of the lesion, and, in some cases, the size of the lesion, as expressed in the roentgenologic, surgical, or necropsy reports, are listed. Table 3 gives a comparison of special electroencephalographic features.

In 2 of the 18 cases, the electroencephalogram can be regarded as normal or borderline normal. In both cases the leading symptoms were Jacksonian seizures of rather long standing. In a third case the routine

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TABLE 1.—*Classified Electroencephalographic Findings in Eighteen Cases of Cerebral Angioma*

Normal electroencephalogram (or minimal bilateral abnormality)	Group 1 2 cases	Low-voltage bi-Sylvian theta waves during hyperventilation and photic stimulation Flat record: minimal driving asymmetry; voltage down on side of lesion
Moderate electroencephalographic changes	Group 2 Suggestive of false lateralization	Routine electroencephalogram within normal limits: Pentylenetetrazol activation: Bi-Sylvian theta waves, more marked on side opposite lesion
	2 cases	Bi-Sylvian isolated theta waves, more frequent and higher voltage on side opposite lesion
	Group 3 Suggestive of correct lateralization (3) or localization (2)	3 records: Low-voltage bilateral delta activity with one-sided predominance Low-voltage focal activity in delta and theta range on side of lesion
	5 cases	Diffuse generalized and low-grade focal theta activity; history of subarachnoid hemorrhage 10 yr. previous to recording
Marked focal electroencephalographic changes, diagnostic of correct localization	Group 4 Without history of recent subarachnoid or intracerebral hemorrhage or both	2 records: Recorded seizure with postictal high-voltage slow-wave focus Rhythmic and arrhythmic focal and hemispheral delta waves recorded 20 yr. after craniotomy
	6 cases	Delta focus: Multiple neck arteries ligated 14 yr. prior to electroencephalogram Focal abnormalities in delta and theta range Marked delta focus: First electroencephalogram recorded two yr. after exploratory craniotomy
	Group 5 With history of recent subarachnoid or intracerebral hemorrhage or both	High-voltage delta foci on side of lesion
	3 cases	

TABLE 2.—*Correlation of Electroencephalographic Features with Historical, Neurologic, and Pathologic Features*

Group of Cases (See Table 1)	No.	Age of Onset, Yr.	Duration of Symptoms Before Electroencephalography, Yr.	Findings on Neurologic Examination	Seizures (Type)	Location and Size of Lesion
1	1	29	9	C.N.S. negative	Rt. Jacksonian	Lt. frontoparietal
	2	22	13	C.N.S. negative	Rt. Jacksonian	Lt. parietal: Large
2	3	25	5	Stereognosis impaired on lt.; slight drop lt. buccal angle	Adversive seizures to left	Arteriovenous fistula rt. anterior cerebral artery to superior sagittal sinus
	4	34	6	C.N.S. negative	Temporal-lobe seizures	Lt. posterior parietal: Large
3	5	24	17	C.N.S. negative	Generalized convulsions	Rt. frontal: Large
	6	13	10	Bruit; engorged retinal veins	Adversive seizures	Rt. frontal: Large
	7	3	12	Rt. homonymous hemianopsia	.....	Lt. occipital: Large
	8	60	1	Transient, recurrent lt. homonymous hemianopsia	Temporal-lobe seizures	Deep rt. parietal: Large
	9	17	11	C.N.S. negative; calcification deep rt. frontal area	Generalized convulsions	Rt. frontal: Large
4	10	35	1	Dilated lt. pupil	Temporal-lobe seizures	Lt. posterior temporal
	11	18	20	C.N.S. negative	Temporal-lobe seizures	Lt. posterior temporal
	12	3	22	Lt. hemiparesis	Lt. Jacksonian	Rt. hemispheral
	13	9	28	Lt. homonymous hemianopsia	Lt. Jacksonian	Rt. posterior parietal
	14	48	1	C.N.S. negative	Generalized convulsions	Lt. Sylvian: Small
	15	24	3	Rt. choked disc; bruit	Generalized convulsions	Lt. frontal
5	16	33	6 wk.	Bilat. choked discs; aphasia rt. lower quadrant hemianopsia	.....	Lt. posterior temporal + parietal (hemorrhage)
	17	16	6 days	Rt. hemiparesis; stiff neck; aphasia	.....	Intracerebral hemorrhage lt. parietal
	18	32	3 wk.	C.S.F. bloody	.....	Rt. occipital: Large

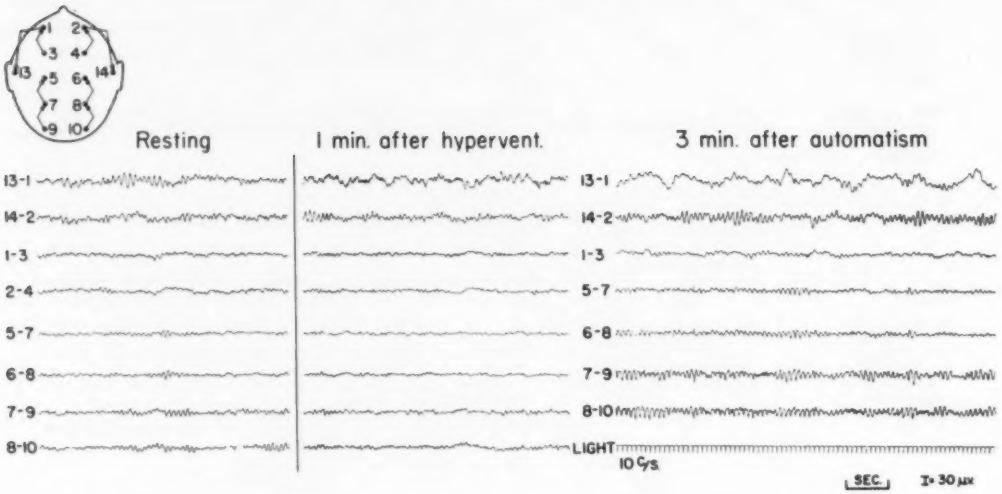

Fig. 1.—Left Sylvian slow-wave focus three minutes after an automatism, which occurred after the three-minute period of overbreathing. Left carotid angiography revealed a left temporoparietal arteriovenous anomaly.

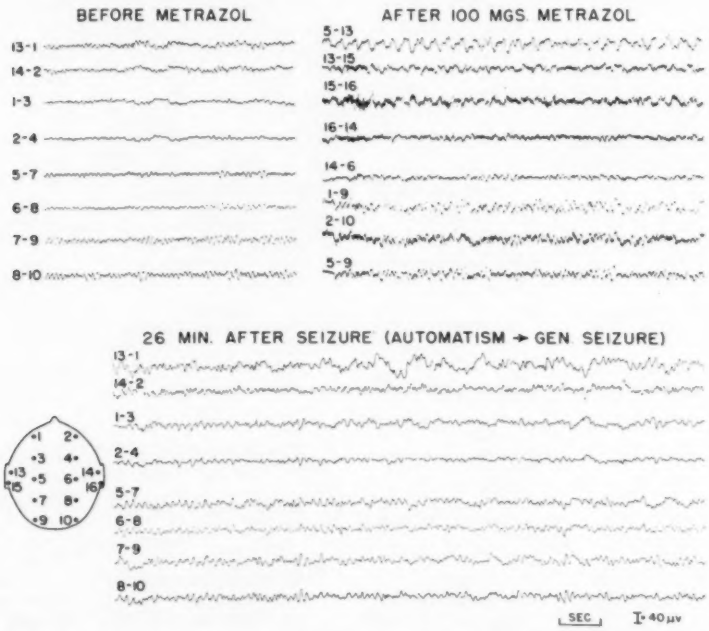

Fig. 2.—Left Sylvian slow-wave focus 26 minutes after a recorded automatism with a subsequent generalized convulsion, occurring in the course of a pentylenetetrazol-activation study, when a total of 650 mg. had been administered by the intravenous route. Transient focal left Sylvian activation after 100 mg., unaccompanied by clinical manifestations. Left carotid angiography revealed an extensive left temporoparietal arteriovenous anomaly. Note the minimal preictal electroencephalographic changes.

recording showed minimal bilateral changes of the slow-wave variety. Because of the history of adversive seizures to the left and left-sided neurologic findings, a pentylenetetrazol activation was carried out. A seizure, however, was not induced, and the electroencephalogram showed isolated medium-voltage bi-Sylvian sharp discharges, with predominance on the side opposite the lesion, which was found to be a fistula from the right anterior cerebral artery to the superior sagittal sinus. In another case, with a six-year history of temporal-lobe epilepsy and negative results of neurologic examination, isolated waves with a sharp contour were most persistent and predominant on the side opposite the lesion.

Epilepsy was the leading symptom in four of five patients in Group 3. The history was comparatively short in only one case, the age of onset being between that of 3 and 60 years. The electroencephalographic findings gave correct lateralization in three cases and correct localization in two cases. In one case there was a history of subarachnoid hemorrhage 10 years prior to the recording.

In two of the six cases in Group 4 a cranial operation had been performed prior to the electroencephalography, and in one case repeated ligations of multiple neck and cranial arteries had been performed. Two more cases in this group showed marked focal electroencephalographic changes only during and after a convulsive seizure, which in one case occurred after the hyperventilation period and in the other case was induced by intravenous injection of pentylenetetrazol. In the first case the preictal tracings showed only moderate changes, consistent with the criteria applied in the selection for Group 3 (Fig. 1). The routine recording and the preictal tracing in the second case were borderline normal (Fig. 2). Thus, there remains only one patient in Group 4 whose resting record showed focal localizing abnormalities. In this case the history was comparatively short and the results of neurologic examination were negative.

Three cases of recent subarachnoid hemorrhage were listed in Group 5. The electroencephalogram was first recorded between six days and six weeks after the presumable occurrence of the hemorrhage. In spite of the fact that the primary lesion may be an added factor in electroencephalographic changes after subarachnoid hemorrhage, a point stressed by Walton,[2] it was felt that the recent occurrence of this complication in our cases was probably responsible for the drastic electroencephalographic changes. In two of the patients a large intracerebral hematoma was encountered and removed. In the third case angiography revealed a large occipital arteriovenous anomaly. The patient was treated conservatively, and therefore it cannot be determined whether intracerebral hemorrhage had occurred also here. Clinically, this patient complained only of headaches and a stiff neck. The cerebrospinal fluid was bloody. In this connection, it is interesting to note that in roughly 50% of patients with subarachnoid hemorrhage some degree of intracerebral bleeding occurs, which remains often without clinical evidence (Walton,* Robertson [3]). The electroencephalographic features in our three cases were very much alike in spite of a wide variation of clinical manifestations. High-voltage, random delta waves of 1 to 3 cps, not inhibited by eye opening, were recorded in each case over a rather wide field of one hemisphere. In all three cases there was a marked alpha asymmetry with disorganization and suppression of the alpha rhythm on the side of the lesion. The response to rhythmic photic stimulation showed a corresponding asymmetry. Lateralization was correct in all three cases.

Postoperative Electroencephalographic Changes.—In five of the six cases in which postoperative electroencephalograms were available the electroencephalogram had also been recorded preoperatively. The postoperative recordings were taken from 2 weeks to 26 months after operation. Analysis of these records showed that the degree

* Walton, J. N.: Thesis, Graduate School, University of Durham, Durham, England; cited in Walton.[2]

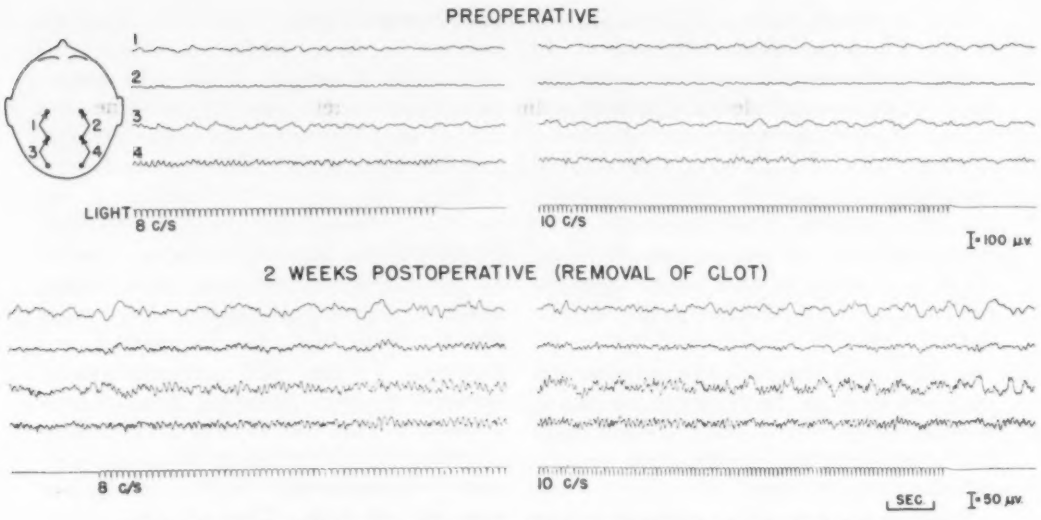

Fig. 3.—Recovery of flicker response two weeks after resection of a left parietal arteriovenous varix and removal of an intracerebral hematoma. Marked postoperative clinical improvement.

of postoperative electroencephalographic changes depended on the type of procedure carried out, as well as on the time elapsed since the operation, and to some extent also on the kind of intracranial lesion encountered. Operations with extensive removal of the underlying lesion had been done in three patients. In these cases persistent, focal, high-voltage delta waves were present in the tracings, which were taken from 2 weeks to 10 months after surgical intervention. In the other three cases operation consisted either of trapping procedures or of exploration only. In these cases the electroencephalogram showed focal changes, differing markedly from the preoperative recording. The focal abnormalities were of the delta variety in three records of two patients obtained from 2 weeks to 24 months following operation, and of the sharp-wave variety in one case taken 26 months postoperatively. All electroencephalographic changes in the latter group, however, were much less marked.

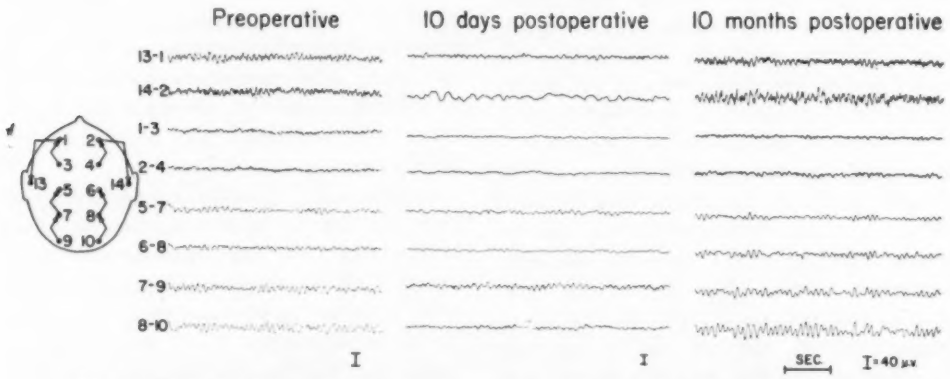

Fig. 4.—Right Sylvian random slow-wave focus and ipsilateral alpha depression 10 days after a trapping procedure for a right parietal-parasagittal arteriovenous anomaly in a patient with adversive seizures to the left. The marked improvement of the tracings 10 months postoperatively, with return of alpha rhythm over the right side, did not correspond to the clinical course, which was characterized by an increase of the focal seizures. Carotid angiography showed reestablishment of abnormal vascular channels.

It appears that random slow-wave activity predominates in all records taken in the immediate postoperative period. Skull defects following craniotomy make it difficult to evaluate the change or appearance of alpha and photic-driving asymmetries. In one patient with extensive surgery who showed marked clinical improvement within two weeks after the operation, return of alpha rhythm and of response to photic stimulation was noted on the side of the lesion (Fig. 3). In another patient there was an ipsilateral depression of alpha rhythm and driving 10 days following a trapping procedure for an arteriovenous varix. Ten months postoperatively the focal abnormalities of the electroencephalogram had improved, and alpha voltage was greater on the side of the operation, whereas the driving response had again become symmetric on the two sides. Clinically, however, this patient had become worse, and carotid angiography carried out at this time showed some reestablishment of abnormal vascular channels (Fig. 4). In the majority of the cases discussed here there was a definite increase of the alpha voltage on the side of the previous lesion, starting 10 months after operation or later.

It can be said that in this group postoperative decrease in the focal abnormalities, together with return of the alpha rhythm and a response to photic stimulation on the side of the lesion and cranial operation, was not necessarily associated with over-all clinical improvement.

COMMENT

Even if the electroencephalogram in cases of arteriovenous anomalies showed the reliable focal alterations seen in case of cerebral neoplasm, its place would still be that of a mere preliminary screening test, owing to the fact that the most important information about arteriovenous anomalies can be supplied only by preoperative angiography. A positive electroencephalogram would be of definite value to the clinician mainly in cases in which the presence of some type of vascular lesion is not already clearly demonstrated or strongly suggested by the history or the findings on examination, and in which the symptomatology leaves the clinician a considerable choice as to the presumable etiology. In cases without lateralizing clinical findings it could be of help in selecting the side of angiography. It could be of value in cases in which one is for various reasons hesitant to rely on angiography a priori. There is no definite agreement in the literature on this subject. Gillingham[4] has stated that the electroencephalogram is not particularly helpful in the differential diagnosis of cerebral angioma, a normal recording being not unusual. Rosenberg,[5] on the other hand, in his analysis of 52 preoperative records, found a localizing or lateralizing indication in 67% of the cases. In 18 of his cases there was a history of subarachnoid hemorrhage. He divided the 52 cases into three main groups, applying criteria similar to those used in this study. Seventeen records showed severe unilateral changes, two of them on the side opposite the lesion. Eighteen records showed mild unilateral abnormalities, mild asymmetries, or activity of 4 to 7 cps. The rest had normal or doubtfully abnormal recordings. Rosenberg reached the conclusion that electroencephalographic alterations in cases of angioma are similar to those seen in cases of cerebral tumor.

In our analysis of 18 cases, moderate focal changes in 5 cases and pronounced focal changes in 9 cases pointed to the correct side, with 2 false lateralizations. In order to determine the value of preoperative electroencephalograms in cases of uncomplicated angioma, cases with a history of intracranial hemorrhage, with cranial operation of some type or with carotid ligation prior to the recording, had to be excluded. Of the remaining 11 records, only 1 showed marked focal changes during the resting electroencephalogram, and 2 more during and after a recorded seizure. Thus, more than half of the records fall into the group of moderate electroencephalographic changes, with two false lateralizations.

The clinical interpretation of this type of record is, unfortunately, often of little or no help to the clinician, since it can be seen

in such a wide spectrum of conditions, ranging from a small portion of the asymptomatic normal (control) group to atrophic or degenerative lesions of the brain to huge angiomas, as shown here.

Walton [2] has suggested that small angiomas are unlikely to produce any changes in the electroencephalogram, whereas a large angioma may itself be of sufficient size to affect the record. In our group no significant correlation could be found between the size of the lesion and the degree or type of electroencephalographic abnormality. In fact, in the only case with marked focal changes in the resting electroencephalogram out of this entire group of 11 records, the alteration was apparently caused by a small left Sylvian arteriovenous varix; and in another case, with a large posterior parietal lesion, the electroencephalogram showed only bilateral changes in theta range, stronger on the opposite side.

Interesting are the two cases of postictal slow-wave focus. The preictal recording was inconclusive in both instances. Pentylenetetrazol activation reproduced a typical automatism, followed by a generalized convulsion in one case. Well-defined spike and sharp-wave activity during the focal part of the seizure and a persistent postictal slow-wave focus gave the correct localization (Fig. 2). In the second case an automatism occurred shortly after hyperventilation. Rhythmic high-voltage waves of 6 to 7 per second during, and a persistent slow-wave focus after, the seizure gave the correct localization of the lesion in this case also (Fig. 1). In another case, pentylenetetrazol activation was carried out, but with the amount given no seizure could be induced. The various aspects of the phenomenon of the postictal slow-wave foci are at the present time under investigation at this institution.

In view of the limited clinical value of routine electroencephalograms in cases of uncomplicated angioma, and in view of the high localizing value of ictal and postictal focal electroencephalographic changes, pentylenetetrazol activation, with the aim of inducing a seizure, should be used more frequently in a selected group of suspected cases, especially when there is a history of seizures.

Persistent pulse artifact obtained from scalp areas directly overlying the angioma was reported by Chavany, David, and Lerique [6] (1949) and by Floris and Mengoli [7] (1949). No such case was found in our group. In 14 of our patients there was a history of epilepsy, the majority of whom did not show the typical, specific electroencephalographic changes. This finding corresponds to Rosenberg's [6]; in his group 34 patients had a history of epilepsy with little bearing on the electroencephalographic changes. The results of neurologic examination were negative in five patients in Groups 1 to 3 and in two patients in Groups 4 and 5. In 12 of the 18 cases the onset of symptoms was before the age of 30 years, the earliest manifestations being at the age of 3 years, the latest at 60 years. Analysis of postoperative records confirmed the impression of Rosenberg, who did not find any definite correlation of the clinical state with the electroencephalogram. Investigation of special electroencephalographic features does not reveal any significant increase or decrease of alpha rhythm and driving response on the side of the lesion in the uncomplicated cases. Alpha rhythm and driving response were deteriorated in all three cases of recent subarachnoid hemorrhage. There was an increase of the abnormalities during hyperventilation in 9 of the entire group of 18 cases (Table 3).

TABLE 3.—*Comparison of Some Electroencephalographic Features*

	Groups 1 and 2 (4 Cases)	Group 3 (5 Cases)	Group 4 (6 Cases)	Group 5* (3 Cases)
Alpha asymmetries				
Decreased on side of lesion	..	1	1	3
Increased on side of lesion	1	..	1	..
Hyperventilation				
Increase of abnormalities	..	5	3	1
Driving response				
Decreased on side of lesion	1	1	1	3
Increased on side of lesion	..	1	1	..

* Selection of groups: See Table 1.

SUMMARY

A detailed analysis of the electroencephalogram in 18 patients with arteriovenous anomalies of the brain indicates that the diagnostic value of the electroencephalogram in evaluating suspected cases is limited.

Low-voltage bilateral abnormalities in theta or delta range with one-sided predominance were found in the majority of arteriovenous anomalies recorded prior to intracranial operation or intracranial hemorrhage. In this group the electroencephalographic alterations appeared to be similar to those frequently seen in cases of atrophic or degenerative lesions of the brain.

No correlation was found between the size of the lesion and the degree of electroencephalographic alteration.

In view of the limited clinical value of routine electroencephalography in suspected angioma and of the high localizing value of ictal and postictal focal electroencephalographic changes, the more frequent use of activation methods to induce a seizure is suggested.

In three cases of subarachnoid hemorrhage secondary to angiomatous lesions, high-voltage delta foci were found on the side of the lesion.

Analysis of postoperative recordings did not reveal any significant correlation between clinical and electroencephalographic status.

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News and Comment

ANNOUNCEMENTS

A. M. A. Annual Meeting, Chicago, June 11-15, 1956.—The 105th Annual Meeting of the American Medical Association will be held in Chicago, June 11-15, 1956, with a full program of lectures, television, motion pictures, and scientific exhibits.

The lecture program for each Section is prepared by the Section Secretary, and prospective participants should communicate as soon as possible with the Secretary of the Section before which they hope to read a paper. Application blanks for space in the Scientific Exhibit are now available and may be obtained from the Section Representative to the Scientific Exhibit.

Section on Nervous and Mental Diseases

Secretary: Karl O. Von Hagen, M.D., 2010 Wilshire Blvd., Los Angeles 57.

Exhibit Representative: G. Wilse Robinson Jr., M.D., 2625 W. Paseo, Kansas City 8, Mo.

Additional information may be obtained from the Secretary, Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10.

Cortical Inhibition in Expressive Aphasia

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and
JOAN LEE, B.A., New York

Expressive aphasia has most generally been considered to be a loss in expressive language function as the consequence of destruction or damage of the cerebral cortex. While there has been considerable agreement concerning the facts of brain damage, substantial disagreement has attended attempts to define the mechanisms by means of which cortical destruction results in a disruption of speech and language. Explanations of mechanism have ranged from extreme localization theories, in which specific cytoarchitectonic areas have been identified as the loci of various expressive language functions, to general functional theories, such as that of Goldstein,[1] who argues in terms of the general reorganization of cortical properties and the modification of general psychological attributes.

In the course of working with a population of patients with expressive aphasia over a period of years, it appeared increasingly to us that too much attention had been devoted to the negative symptoms (i. e., loss of expressive language) in the elaboration of theories, and that an adequate theory could only be approached through a more careful analysis of positive symptoms (i. e., the nature of expressive functions that were retained by the patient). When attention is so directed, it becomes clear that the arrest of expressive language function in patients with emissive aphasia is rarely absolute. On the contrary, such patients often exhibit the ability to express themselves orally in limited and specific ways and under certain explicit circumstances. Thus, one patient may be able repetitively to enunciate "I don't know!" but not to speak other words or sentences. Another patient may be able to speak words as such but not to select and use the word or words which are appropriate to the situation. Yet another patient may not be able to name an object when it is presented but is capable of repeating the name after the therapist has said it. On other occasions a patient who is almost mute does shout out an expletive when in pain or on other occasions shows interjectional speech. Such phenomena suggest strongly that expressive aphasia cannot always be considered as a loss of motor-speech function, but, rather, must be viewed as an omnibus disorder in which traumatic alterations in cortical circumstances have modified the normal patterns of excitation. It suggests further that in many cases the disruption of expressive language functioning is a consequence of an altered relationship between the motor-speech projection region and the remainder of the cerebral cortex, and not a subtractive loss in motor-speech projection as such.

When viewed in this manner, many of the symptoms found in motor-aphasia patients are strikingly reminiscent of phenomena described by Pavlov[2] in his effort to define the physiological relations in the cerebral

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cortex by means of the study of conditioned reflexes. In particular, one is struck by the resemblance of such phenomena as (1) extinction; (2) internal, conditioned and external inhibition, and (3) disinhibition in the conditioned reflexes to such phenomena as mutism, blocking, inappropriate naming when stimuli are presented in the visual modality, and interjectional or expletive speech found in the aphasic patient. Such a resemblance suggests the possibility that many of the symptoms of dysfunction in the motor-aphasia patient are the consequence of a disordered cortical relationship in which the cortical damage has contributed to the development of an inhibitory system involving the motor-speech projection area.

If one hypothesizes that cortical inhibition, and not a subtractive loss in functional capacity, underlies many of the manifestations of expressive aphasia, it follows that the symptoms may be markedly relieved by creating circumstances for facilitating disinhibition. In the experimentation on the conditional reflexes it has been shown by Pavlov and his associates that disinhibition may be produced by three types of events. The first of these is the reinforcement of the inhibited conditioned reflex by the application of the original, or unconditioned, stimulus. The fact that often the patient with motor aphasia is able to name an object or "say" a word once the therapist says it, but not in response to the visual stimulus, is a fact congruent with the method of unconditional stimulus reinforcement. A second procedure for producing disinhibition in the experiments on the conditioned reflex is the introduction of a strong, though irrelevant, stimulation. It appears that the phenomena of expletive and of interjectional speech may be the consequence of this kind of disinhibition. The third method for achieving disinhibition in the conditioning studies involves the determination of the cortical activity which is producing the inhibitory effect and inhibiting it. Thus, disinhibition may be produced through inhibiting the inhibitor. It is this third aspect of the phenomena of disinhibition which was investigated in the present study.

From both the anatomic evidence in expressive aphasia and scattered items of evidence in the field of speech therapy a tentative formulation of a possible inhibitory process could be made. The anatomic and physiologic evidence points to the fronto-temporal complex as the region of language vulnerability. This anatomic organization, when taken together with the facts that high-intensity auditory stimulation reduces stammering and stuttering, while out-of-phase auditory input of spoken language induces blocked speech or motor-speech disruption, suggests that if an inhibitory process underlies certain varieties of expressive aphasia, the likelihood is high that it is either the auditory projection or the association process which is inhibiting the motor-speech projection system. If this is indeed the case, then it follows that expressive language function should be improved by the elimination of such an inhibitory process. Such release from inhibition can most easily be accomplished by dominating the activity of the auditory projection system through the application of a prolonged, continuing, strong stimulus. These considerations led to the elaboration of the following experiment.

PROCEDURE

Fourteen right-handed patients suffering from severe forms of expressive aphasia were selected to participate in the study. All of them had had cerebral vascular accidents and were left with residual right hemiplegia and expressive aphasia. The patients had all been given standard speech reeducation therapy for periods of 6 to 18 months, with minimal positive results. The duration of illness ranged from a minimum of two years to a maximum of five years. The patients were asked to (1) name objects, (2) name objects from pictures, (3) read single words aloud, and (4) read connected sentences aloud, each under two conditions. In condition A no extraordinary stimulation was presented. Patients sat in the quiet therapy room and were presented with the tasks listed above. In condition B the same tasks were presented, but 30 seconds before the presentation and throughout the entire series of presentations a tone of 256 cps at an intensity of 60 db. was binaurally administered. This

intensity of auditory stimulation is sufficient to make a loud shout inaudible but is below the pain threshold for almost all patients. In all cases auditory stimulation was delivered through a pair of headphones that were activated by the masking tone of an audiometer.

RESULTS

When the patients were asked to perform without added auditory stimulation, they all showed marked difficulty in one or more of the tasks. Some subjects could name objects but not the pictures of objects. Others could not name objects or the pictures of objects but could read single words aloud, and even short sentences. In all cases the latency of verbal response was very long and the response made was frequently inappropriate to the stimulus presented.

When the same tasks were presented with accompanying binaural auditory stimulation, a marked change in performance could be observed. In 10 of the 14 patients tested, performance was decisively improved. Four patients showed no differences in performance under the new conditions of testing. In the 10 patients who exhibited an improvement under the "noise" condition the following changes were noted:

Patients who could not same a single object in the room under the "quiet" testing condition quickly and readily named such objects as "chair," "table," "man," "sink," "door," or "wall." Test pictures, such as an apple, a train, a saw, a chicken, and a boy, which could not be named under the "quiet" condition, were consistently and correctly identified with binaural "noise" stimulation. Patients who could not read single words aloud when tested in the "quiet" circumstance exhibited such an ability on auditory stimulation. Patients who could read aloud only short (3-to 4-word) sentences in the "quiet" condition could readily read double this amount aloud with "noise." In all 10 subjects the latency of verbal response to presented stimuli was more than halved when they were given auditory stimulation. Enunciation under "noise" stimulation was decidedly improved. The responses of Patient M. W. which follow are typical for the group showing improvement.

Task 1: Naming of pictures

	Responses	
Pictures	"Quiet"	"Noise"
Apple	"I don't know"	Apple
Saw	Same	Saw
Chicken	Same	Chicken
Train	Same	Train
Boy	Same	Boy

Task 2: Reading sentences

"Quiet": Subject could read 4-5 words and then stopped or lapsed into irrelevant wording or muttering.

"Noise": Subject could read up to 20 words in a connected passage.

It is of interest to note there was some residual after-effect when the auditory stimulation was discontinued. This after-effect persisted for from 5 to 10 minutes after the first administration of auditory stimulation and resulted in the continuation of improved function. After 10 minutes the patients returned to their original status. However, upon repeated trials the length of the after-effect period tended to be prolonged for several hours and a cumulative residuum of improved expressive language functioning developed. These and other data will be presented in a subsequent report, which is in preparation.

COMMENT AND CONCLUSIONS

It is felt that the results of the investigation affirm the fruitfulness of the theoretical analysis which conceptualized expressive aphasia as the consequence of an inhibitory rather than as a subtractive defect. However, since all patients did not show improvement as the result of auditory stimulation, the possibility of subtractive defects most certainly is not excluded by the results obtained. Still another possibility not excluded by the data is that in the patients whose speech is not positively affected by auditory stimulation an inhibitory relationship may exist but may not involve the auditory projection system. This possibility is supported by some fragmentary evidence obtained by introducing strong kinesthetic stimulation.

However, much work has still to be done before any definitive conclusion is possible.

The results found in the present study have certain practical, diagnostic, and therapeutic implications, in addition to their theoretical significance. It can be tentatively suggested that binaural auditory stimulation can be utilized as a valuable adjunctive procedure in the reeducation of motor-aphasia patients. The possibility exists that by conditioning the auditory stimulation to a clenched hand or to some other self-applied stimulus, the auditory effect may be carried over on a conditioned basis to circumstances in which the auditory stimulation is not present. Further, the data reported lay the basis for a new and more process-oriented diagnostic procedure in the expressive aphasias. These, as well as many other, implications of the present study are currently being investigated and will be presented in subsequent reports.

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Reserpine

Alone and As an Adjunct to Psychotherapy in the Treatment of Schizophrenia

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This paper is a report on a controlled study which extended over a period of eight months using the drug reserpine. Reserpine (Serpasil) offers many of the advantages of present pharmaceutical techniques without incurring many of the liabilities. It acts as a tranquilizer, quieting the patients but leaving their sensorium clear and clouding consciousness but little. Its primary use appears to be in quieting agitated and disturbing patients. We feel that it in no way affects the psychosis itself.

The most exacting test of the effectiveness of this drug would be in using it with chronic, severely disturbed and agitated patients who had failed to improve under the usual regime of treatment, such as insulin coma therapy and electroconvulsive therapy. This would be not only a definitive measure of drug effectiveness but also the most reliable measure. Any improvement shown could then definitely be considered a result of the treatment, since a spontaneous remission would appear highly unlikely. In dealing with acute schizophrenic reactions of short duration it is frequently difficult to determine whether the treatment was a necessary and sufficient cause of the improvement or whether the improvement would have occurred anyway.

Also, this experiment provided an opportunity to determine whether treatment per se, regardless of type or method, would result in any change, preferably for the better. This opportunity was afforded by the fact that the ward from which the subjects were chosen had no formal treatment program in progress because of the severe shortage of personnel. Up to the beginning of this experiment there was only one psychiatrist for 160 patients, and even then he had other duties to perform elsewhere. This service was one housing the chronically disturbed patients. Thus this ward provided the severest test of the drug. The fact that no formal treatment program existed provided the opportunity to measure the effectiveness of treatment per se, regardless of type. The treatments chosen for investigation were reserpine administration, group psychotherapy, a combination of these two, and administration of a placebo (sodium bicarbonate).

METHOD

Thirty-two chronic, severely disturbed and agitated schizophrenic patients residing on the maximum security ward were selected for the experiment. They were assigned to one of four groups of eight patients by the ward psychiatrist. A hospital employee, unfamiliar with the patients, then decided which group would get which type of treatment. Group A received group psychotherapy and reserpine; Group B received group psychotherapy and a placebo (sodium bicarbonate); Group C received only reserpine, and Group D remained as usual, serving as the control group. In the course of the experiment one patient was lost from Group C for refusing to take the drug. After being placed in one of the four groups, each patient was then rated by two psychiatrists on the Lorr Multidimensional Scale for Rating Psychiatric Patients. Each patient was also rated by two

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ward attendants on a seven-point behavioral rating scale devised for this purpose and independently checked for reliability.[2] All patients were given the following psychological tests: Bender-Gestalt, H-T-P, H-T-P chromatic, self-concept drawing, a sentence completion test, and a modified form of the TAT. This testing was repeated at the completion of the experiment, six months later.

The data referring to age, behavioral rating, and length of hospitalization for each group are summarized in Table 1. All the patients had previously received insulin coma therapy and electroconvulsive therapy, with no remarkable improvement. In each group there was one patient who had received a lobotomy. All of these patients were considered chronically disturbed.

Medication was started on Aug. 23 and ended on Feb. 25. The patients were started on 1 mg. per day, and dosage was adjusted thereafter according to the behavior of the patient. The maximum dose was 8 mg. per day; the average dose was 4 mg. per day at the completion of the experiment. There have been no remarkable side-effects.

TABLE 1.—*Mean Age, Behavioral Rating, and Length of Hospitalization*

Group	Age, Yr.	Behavioral Rating	Hospitalization, Mo.
A	38.5	2.7	54
B	31.9	3.4	50
C	38.1	3.3	60
D	33.9	2.4	71

All the patients have had blood studies, and no change in the hematology has occurred.

The group psychotherapy sessions were held three times per week, one hour per session. There were two therapists, a staff psychologist, and a clinical psychology trainee. The therapy was aimed primarily at inducing behavioral changes. It attempted to get the patients to express themselves in a way that was personally satisfying and socially acceptable. The methods used to obtain the changes varied from being very directive, and at times punitive, to being completely accepting and nondirective. This varied according to the individual patient, and the approach depended on determining the individual needs, defenses, and stresses operating on the patient. The most difficult aspect of therapy with patients of this type was in getting them to function as a group; there was a marked tendency for each patient to try to dominate the attention of both therapists. This rivalry was taken advantage of and led to the patients communicating with each other as well as with the therapists. At no time was any assaultive behavior permitted while therapy was in session; this limit was firmly impressed on the patients, since such behavior was not uncommon. Interpretations were made very sparingly, and then they dealt with immediate behavior and feeling. No attempt was made to interpret in a dynamic or historical sense or to provide insight to the patient.

The measurements of improvement were purely behavioral, only one of which required the subjective clinical judgment of any of the professional staff members. They were as follows:

1. Ratings by two staff psychiatrists on the Lorr Multidimensional Scale.
2. Ratings by two ward attendants on a seven-point behavioral rating scale. These ratings were made one week before medication began and again on the day medication was stopped, six months later.
3. Decline in number of neutral wet packs.
4. Decline in number of times placed in room seclusion.
5. Decline in number of fights engaged in.
6. Decline in number of disturbed reports made by the nurses.
7. Transfer to a better ward requiring a higher level of integration.
8. Discharge from the hospital.

The number of packs, room seclusions, fights, and disturbed reports were determined for the six months prior to treatment and compared with the six months during which the patients received treatment. All of the above are objective behavioral measures, since no dramatic changes in personality structure were expected to occur over a period of six months.

RESULTS

The original ratings of the patients by the two psychiatrists on the Lorr Multidimensional Scale were so divergent that they were eliminated from further consideration. The differences between the pre- and postbehavioral scale ratings by the two ward attendants were first considered. The rating used for tabulation was the mean of the ratings by the two attendants. A parametric analysis of variance for the four groups yielded an F value of 0.49 for 3 and 24 degrees of freedom, which is not significant. The Kruskall-Wallis test, a nonparametric analysis of variance, gave a χ^2 of 3.18 and for 3 degrees of freedom was significant at between the 0.15 and the 0.10 point. Thus,

although the degree of change from group to group was not significant, the nonparametric anova (analysis of variance) strongly suggests that the direction of the change was more consistent in some groups.

Of the six parametric *t*-tests among all groups, only one approached significance. This was a *t*-value of 1.66 for the difference between the therapy-plus-drug group and the control group, which for 12 degrees of freedom has a *P* value between the 0.10 and the 0.05 point.

In analyzing the data referring to the number of packs, room seclusions, fights, and disturbed reports, Wilcoxon's nonparametric *t*-test for paired replicates was used along with a χ^2 to compare the six months before treatment with the six months following its introduction. These results, as presented in Table 2, appear quite spectacular. Group A showed a significant improvement on all of the measures, while the control group (Group D) remained practically the same. The other two groups showed significant changes, also but not in all areas. It is to be noted now that the Wilcoxon *t*-test, which is not influenced by extreme cases, does not substantiate χ^2 in all measures. In these cases the significant drop is due to dramatic changes in one or two members of a group. This is discussed later in greater detail. That there did occur definite behavioral changes is more than substantiated by Table 2.

TABLE 2.—*Behavioral Changes as a Result of Treatment*

Group	Measure	Pre-treatment	Post-Treatment	χ^2	Wilcoxon *R*
Drug and psychotherapy (A)	Packs	53	16	19.8*	3.0†
	Seclusion	80	40	13.2*	...
	Fights	30	14	5.8*	1.5*
	Disturbed reports	45	6	29.8*	1.5*
Psychotherapy and placebo (B)	Packs	56	15	23.6*	10.5
	Seclusion	1	0	....	...
	Fights	18	7	4.8†	0.5*
	Disturbed reports	18	1	15.2*	0.5*
Drug only (C)	Packs	48	11	23.2*	7.5
	Seclusion	0	0	....	...
	Fights	13	8	1.2	6.0
	Disturbed reports	39	10	17.6*	0.5*
Control (D)	Packs	73	80	....	8.5
	Seclusion	83	84	....	...
	Fights	30	28	....	16.0
	Disturbed reports	26	21	....	17.0

* *P* value less than 0.01.
† *P* value less than 0.025.

Fisher's exact method was used to determine the χ^2 for test differences among the four groups for each of the seven psychological tests. None of the differences on any of the tests approached significance.

COMMENT

It is obvious from the results presented in Table 2 that dramatic changes took place in the behavior of the three treatment groups. These changes, however, appear to be confined to the behavioral field, since the change was not reflected in the psychological tests or in the behavioral rating scale. That the tests and rating scale do reflect improvement has been shown elsewhere.* None of the treatments was effective in causing any significant personality change; i. e., the schizophrenic process itself was not affected. The manifestation of the psychosis, though, was drastically curtailed. Perhaps this is all one can expect to do at the present state of our knowledge of this illness.

Although all three treatment groups improved significantly, there was a difference in degree of improvement among groups. The group receiving both reserpine and psychotherapy showed the greatest over-all improvement. Also, from this group three patients were transferred to better wards permitting more privileges and implying a higher level of personality integration, as against one each from Groups B and C.

Also, there was a difference in degree of improvement within each group. As mentioned before, there is a discrepancy between the χ^2 and the Wilcoxon *R* in Table 2. The χ^2 is a measure of the difference in the actual number of incidents occurring whether this number is a function of only one patient or

* References 1 and 2.

of eight patients. The Wilcoxon *t*-test, on the other hand, is not influenced by the extreme cases but, rather, is a measure of the consistency of the direction of change within each group. Where the statistics are at variance, the significant χ^2 is a function of a marked change in one or two patients who were relatively more agitated and anxious. In all the treatment groups, the greatest change occurred with those patients who showed the highest level of manifest anxiety, agitation, and a tendency to "act out" their impulses.

Both reserpine and group psychotherapy alone are effective agents for bringing about marked behavioral changes in some chronic, severely disturbed and agitated patients. The greatest improvement occurs when the two treatments are combined. This combination permits the use of the drug to decrease inappropriate defensive activity and the use of the psychotherapy to instigate new, more appropriate and acceptable defenses. Actually, the drug eliminates the early steps of psychotherapy, which is the steady weakening of anxiety attached to any self-inspection. As the therapy sessions deal with anxiety by gradually weakening it through extinction and thus permitting freer expression and introspection, so does the drug act, but in a more precipitate manner.

There is no doubt that the treatment of these patients for six months effected changes. A glance at the control group of Table 2 shows this. However, none improved enough to warrant discharge. Also, if one considers improvement in terms of personality change, then the four groups do not differ as a result of treatment. This is reflected in the lack of any significant change in the psychological testing and behavioral rating scale.

Probably the outstanding factor to be considered is that the greatest improvement occurred usually in the most violent patients. This is partly a result of the means of measurement. Since the measures were in terms of behavior deviations, the more violent patients had more room to improve. However, it also points up the relative specificity of this drug in the type of patient with which it is effective. Theoretically, it suggests that there are different types of patients based on a physiological or biochemical criterion, rather than the present symptomatic nosology. The drug is effective with those patients who still show a predominant adrenergic, rather than a cholinergic, autonomic activity. This would logically follow, since the drug is supposed to operate through the diencephalon, primarily via the hypothalamus.[4] The drug would act as a depressor of the hypothalamus, an effect which, according to Gellhorn,[3] would be advantageous to agitated, anxious patients. However, there is no definite evidence to show that it does act as a depressant of hypothalamic activity. It has recently been theorized that reserpine acts as a facilitator of synaptic transmission, causing an increase of cortical activity (inhibition of diencephalic structures).[5]

In conclusion, reserpine is an effective addition to the available treatments for some types of mental illness. It does not cure the disease of schizophrenia. We wonder whether this drug will not require an additional outlay of funds, rather than a decrease of expense per patient—not that the drug price itself is the main factor; but, rather, that the main function of the drug appears to be in making some patients more amenable to other therapies, thus requiring the addition of these therapies to regular hospital routine. It would appear wasteful to offer the one without the other.

SUMMARY

Four groups of eight severely disturbed, chronic schizophrenic patients were selected by the ward psychiatrist. One group received group psychotherapy and the new drug reserpine; another received psychotherapy and a placebo; the third group received only the drug, reserpine, and the fourth group acted as a control. After six months of treatment, behavioral changes were measured. No significant improvement occurred on the psychological tests. Marked improve-

ment occurred with behavioral measures. The greatest improvement occurred when reserpine was used along with group psychotherapy.

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Epilepsy in Macaca Mulatta After Cortical or Intracerebral Alumina

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A recent publication [1] dealing with the production of epilepsy in the monkey by the intracortical injection of alumina cream has indicated that certain pertinent information and results are apparently not widely known. The technique for production of experimental epilepsy in the monkey by topical cortical disc application of alumina cream was first described in 1942.[2] Thereafter we also reported on the successful use of intracerebral and intracortical injection techniques.* The present communication is intended to present additional data and findings regarding the production of chronic experimental epilepsy in the monkey.

METHODS

Four preparations of alumina have been employed: a standard laboratory alumina (aluminum oxide) cream made according to Hawk and Bergeim,† using sterile solutions and aseptic technique; a commercial product (aluminum hydroxide, gelatinous A-583, Fisher), autoclaved and emulsified with sterile water by means of a Ten Broeck grinder [5]; aluminum oxide,‡ autoclaved and emulsified with water to a granular paste, and Alumina A, prepared in our laboratory.§ The standard alumina cream preparation, stored at 4 C for periods up to two years, was centrifuged before use and the gelatinous sediment used. Representative samples ignited to Al_2O_3 with a Meeker burner contained 3 to 14 mg/ml. equivalent of aluminum. For example, two preparations each yielded values of 9 mg/ml. when centrifuged at 2600 rpm (1500 g) for 15 minutes, and 13-14 mg/ml. at 3200 rpm (2250 g) for two hours. Alumina A (2600 rpm for 15 minutes) contained an equivalent of aluminum of 32 mg/ml. One of the two commercial preparations which was analyzed (A-583) was employed in concentrations containing 5 to 24 mg/ml. of aluminum.

For injection, a 26-gauge hypodermic needle was generally employed, or on occasion a 21-gauge needle. Injections were usually performed under direct visual control with dura incised and retracted and cortical surface exposed. Since reflux of injected material occurred occasionally, the volume retained was estimated. Injections were made either at single or at multiple sites in one or both cerebral hemispheres into the cortex and superficial underlying white matter of the sensorimotor zones with the needle inserted to a depth varying from 3 to 10 mm. from the cortical surface. In the case of 10 monkeys [4] injection of alumina cream was carried out through a 26-gauge needle placed by means of a Horsley-Clarke stereotaxic instrument into various subcortical sites. In two monkeys 0.1-0.25 ml. was injected subcortically to a depth of 5-6 mm. beneath the site of a previous cortical ablation. Two control monkeys received eight intracortical injections of either an Aquaphor (oxycholesterol-petrolatum) emulsion (1 part Aquaphor: 2 parts saline) or isotonic saline into a sensorimotor cortex. Pertinent data regarding location, number of sites, depth, etc. are included in the accompanying Table.

The use of discs for topical application has been described.[2] Discs containing the standard laboratory preparation of alumina cream were employed in 154 monkeys, commercial alumina (Fisher) in 4, commercial aluminum oxide paste in 3, and Alumina A in 3. One monkey received a smaller-size disc con-

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† Hawk and Bergeim,[11] p. 923.

‡ Furnished by Aluminum Ore Co., East St. Louis, Mo., as alumina A-1.

§Hawk and Bergeim,[11] p. 262.

taining the standard laboratory preparation. Discs were left in situ over the sensorimotor cortex during the entire observation period. In two additional monkeys the standard preparation was left in place for one day only, and in two others for one week. Thirty-seven monkeys which were treated by application of discs filled with miscellaneous "inactive" substances served as controls. Included in this group were various metallic oxides and compounds; Aquaphor emulsified with isotonic saline; gelatin, and monkey and rabbit serums, as well as empty discs.

Clinical observations and electroencephalographic recordings were generally made at biweekly or monthly intervals over periods usually ranging from one to three years. Clinical convulsive seizures were precipitated by stress stimulation (stick prodding), as well as by a standard intramuscular test dose of 16 mg/kg. of pentylenetetrazol (Metrazol). Metrazol activation of EEG's following rapid intravenous injection of 0.1-0.2 ml. of 10% pentylenetetrazol and by intramuscular injection of 16 mg/kg. was employed.[7]

Epilepsy in Macaca Mulatta Produced by Alumina

Prep.*	Alumina, Ml.	Location	No. of Sites	Depth of Injection, Mm.†	Clinical Epilepsy, Pos./Treated
Lab	0.1	Motor cortex	1	5	1/2
Lab	0.4	Motor cortex	8	5-8	1/1
Lab	0.2-0.3	Sensorimotor cortex	3	6-7	2/2
Lab	0.3-0.6	Sensorimotor cortex	8-9	3-11	8/9
Lab	0.6-1.2	Same bilateral	16	5-9	1/1
A-583	0.2-0.3	Sensorimotor cortex	10-12	7-8	2/2
Lab	0.35-0.5	Parietal cortex	5-8	5-8	10/10
Lab	0.1-0.25	Motor subcortex ‡	1	6-9	1/2
Lab	< 0.05	Motor cortex	20	1	0/3
Lab	0.1-0.2	Subcortical §	1-2	...	4/10
Control ‖	None	Sensorimotor cortex	8-10	5-9	0/2
			Disc Application		
Lab	0.2-0.25	Sensorimotor cortex	Left in situ		152/154
Lab	0.025-0.03	Same	Left in situ		1/1
Lab	0.2-0.25	Same	Removed after 1 day		1/2
Lab	0.2-0.25	Same	Removed after 7 days		1/2
A-583	0.25	Same	Left in situ		4/4
A-1	0.25	Same	Left in situ		3/3
Alumina A	0.25	Same	Left in situ		3/3
Control ¶	None	Same	Left in situ		0/37

* Lab-centrifuged sediment of standard laboratory alumina cream; A-583 and A-1, commercial products; Alumina A sediment (Hawk and Bergeim,[11] p. 262).
Standard disc: volume 0.2-0.25 ml.; surface area 133 sq. mm.
Small disc: volume 0.025-0.03 ml.; surface area 16 sq. mm.
† From cortical surface.
‡ Beneath previously ablated cortex.
§ Kopeloff and others.[4]
‖ Saline (little retained); Aquaphor-saline emulsion (0.6-0.7 ml. retained).
¶ Miscellaneous "inactive" substances (0.2-0.25 ml.).

RESULTS

Our data indicate that alumina cream injected intracortically, intracerebrally, or subcortically was effective in producing a chronic state of epilepsy in 30 of 42 rhesus monkeys after a latent interval of two and one-half weeks or more. Most responsive areas were in the sensorimotor zone, and injection of a single hemisphere was usually adequate. In animals which became epileptic the estimated amount of alumina cream retained ranged from 0.1 to 0.6 ml. (The aluminum content was estimated as between 0.4 and 5.4 mg. in animals in which the standard laboratory preparation was used.) The epileptic response following multiple injections was characterized by earlier onset (three weeks after injection), resembled epilepsia partialis continua (Koshewnikow) in its initial phase, and was featured by Jacksonian motor convulsions and Jacksonian spread. In three animals in which shallow scarification of 1 sq. mm. of precentral motor cortex was performed through a 0.05 ml. layer of alumina cream, no clinical or electroencephalographic evidence of epilepsy was observed during a period of 13 to 20 months. In the majority of the remaining nonresponsive animals subcortical injection was made into presumably "silent" zones. Two control

monkeys given injections of Aquaphor and saline, respectively, showed no evidence of epilepsy clinically or electroencephalographically and no lowering of threshold to intramuscular pentylenetetrazol over a 9- to 12-month observation period.

The standard laboratory preparation of alumina cream applied in discs left in situ over a sensorimotor cortex produced chronic epilepsy in 152 of 154 monkeys after a seizure-free interval of several weeks or more following operation. Discs similarly applied containing two commercial preparations of alumina, as well as Alumina A, prepared by us, also proved highly effective in 10 monkeys. Two of four monkeys became epileptic when discs containing alumina cream were applied to a sensorimotor cortex for one day or one week and then removed, with onset of seizures 11 and 4 months later, respectively. One animal in which a much smaller disc containing alumina cream was applied to a motor area and left in place also became chronically epileptic.

COMMENT

Our standard laboratory preparation of alumina cream was made according to the method of Hawk and Bergeim,‖ which was based on that of Tracy and Welker [12] and Marshall and Welker.[13] In this method 1% ammonium hydroxide was added to 1% ammonium alum until "finally the liquid yielded a faint odor of ammonia," [13] and then washed by decantation. Other alumina preparations, including Alumina A and several commercial products, have likewise proved effective.

Certain considerations should not be overlooked in attempting to determine a "minimal threshold dose" of alumina cream by injection or disc application. Preparations of alumina cream may vary because of physicochemical differences which are not necessarily related to the quantity of aluminum present. The injection mass is apt to flow back from superficial injection sites, so that injection is best done under direct visual control with estimation of the volume retained. Other factors which might also affect a "quantitative threshold" include the size of the lesion produced, which in our experience varies considerably with similar quantities of alumina cream; the amount of alumina cream present within the injection track; the amount, distribution, and form of aluminum absorbed by contiguous brain; the degree, type, and extent of tissue reaction induced; the area or volume of contact between injection mass and brain; the number and location of injection sites; the method and validation of activating EEG's; the "activity" of the alumina preparation employed and the possible influence of aging; the time interval following alumina treatment; the effective dose concept employed, e. g., $E.D._{.25}$, $E.D._{.50}$, or $E.D._{x}$, and the criteria used for diagnosis of epilepsy.

In 152 of 154 monkeys chronic epilepsy developed after topical cortical application of a disc containing 0.2-0.25 ml. of the standard alumina cream left in situ (equivalent to 0.8-2.25 mg. of aluminum); an additional 10 monkeys similarly treated with commercial alumina or Alumina A preparations also became epileptic. Since, therefore, a total of 162 of 164 treated monkeys became epileptic, it is concluded that the disc method is highly reliable and effective.

SUMMARY

Twenty-six of twenty-nine monkeys injected with alumina cream or a commercial alumina preparation at single or multiple sites in the cerebral sensorimotor cortex became clinically epileptic. Injection into various subcortical cerebral sites produced convulsive seizures in 4 of 10 animals. Minute shallow motor cortex scarification proved negative in three animals.

Topical application by means of discs containing alumina cream, Alumina A, and two commercial alumina preparations left in situ over a sensorimotor cortex was effective in inducing clinical epilepsy in 162 of 164 monkeys. In several instances smaller amounts of alumina cream proved active when either a smaller disc was employed

‖ Hawk and Bergeim,[11] p. 923.

or the standard-size disc was removed one to seven days following application. "Control" preparations were found ineffective.

Factors which might influence the effectiveness of alumina cream in producing epilepsy are briefly cited.

It is concluded that application of alumina cream to the monkey cerebrum either by injection or by topical cortical application is a highly reliable method for the production of chronic experimental epilepsy.

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Body Reflexes Acting on the Body

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Necessity for the array of authors may be understood when one realizes the time consumed by complete neurological studies, especially careful sensory chart, special studies of posture, spasm, and successive reflexes, and selection of suitable patients, who then were studied under water by Dr. Zivin, a procedure later to be described.

Not only in surgery but in many other divisions of medicine, including neurology, a part of the huge debt of death, injury, and disease in war may be compensated by the increment of knowledge resulting from studies made available on a large scale.

This is illustrated by the beautiful studies of Head,[1] Riddoch,[2] and Holmes[3] in World War I.

The monumental contributions of Sherrington[4] and his school, of Magnus,[5] of de Kleijn,* and of Rademaker[6] to reflex activity, especially postural and righting reflexes, afford a background for further studies.

In addition to describing the participation of labyrinthine and neck reflexes in the production of the conventional decerebrate rigidity, or reflex standing, Magnus described certain righting reflexes, the level of whose activities was situated in the midbrain. Among such righting reflexes, he described those which arise as the result of asymmetrical contact stimuli, as when an animal is laid in the lateral position. In the cases we shall describe, the influence of the midbrain, labyrinths, and neck reflexes upon the lower segments of the spinal cord having been eliminated by injury, such reflexes arose from a different source, despite the similarity in stimulus and reaction.

We propose to show that postural changes, both static and kinetic, may be produced in the absence of labyrinthine, neck, or midbrain reflexes.

The material consisted of about 100 veterans with injuries to the spinal cord, in whom the posture varied in respect to the position of the body at rest and the pattern of pseudospontaneous spasm changed in relation to the position of the body at rest; and a special group of 16, who were studied while immersed in water in a swimming pool to diminish the effects of friction and gravity. In cases of injuries to the spinal cord below the level of the first four cervical segments, it was speculated that midbrain, labyrinthine, and neck reflexes had been excluded, and it was later proved to be so by our studies. The comparable state in experimental animals could be found in cats decerebrated by the anemic method described by Pollock and and Davis,[7] with the first four posterior

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* Cited by Magnus.[5]

cervical roots severed and the labyrinths destroyed. The lowermost portion of the anemic area was in the midpons.

Without describing all the reflex activities of such an animal, it suffices to say that there was a marked increase in tendon and nociceptive reflexes. The knee jerks were very active; marked withdrawal, contralateral thrust, and tumultous swipe reflexes were observed.

However, body reflexes acting on the body were preserved, and the muscular rigidity was greater on the side on which the animal was lying on a table, in a lateral position. Among statokinetic reflexes may be mentioned "segmental static reactions." They have been defined as postural reflexes, which also involve the contralateral limb and may be illustrated by the well-known crossed extension reflex. It is probable that the contralateral thrust following an ipsilateral nociceptive stimulus is the result of proprioceptive reflexes. These have also been described in our studies in what are called successive reflexes (Pollock and associates [9]). They are not as simple as flexion and extension alone, but are very complicated and peculiar to each case of injury to the spinal cord. Ipsilateral, as well as contralateral, responses frequently occur. Evidence that these successive reflexes are truly proprioceptive is suggested by the fact that there is an appreciable pause between each particular movement after the first has been provoked by a nociceptive stimulus. Such a series of events may be illustrated by one of many observations.

> Upon stimulation of the sole, there occurred dorsal flexion of the toes and foot, followed after an appreciable time by flexion and abduction of the thigh, with clonic twitches in the muscle groups involved in the movement, and then a contraction of the quadriceps and an extension of the thigh and leg. This was simultaneous with a chronic contraction of the contralateral quadriceps and the adductors and extensors of the thigh.†

Magnus, under the heading of statokinetic reflexes, included the postural reactions of the body in movement.

Somewhat similar are the so-called "associated reactions," described by Riddoch and Buzzard [10] as " automatic activities which fix or alter the posture of a part or parts when some other portion of the body is brought into action by either voluntary effort or artificial reflex stimulation." One immediately thinks of mirror movements in the Klippel-Feil syndrome. The authors call attention to the movements occurring in hemiplegia following yawning, sneezing, and coughing. We (Pollock and others) have described movement of muscles of the upper extremities associated with coughing, yawning, sneezing, and especially inspiration, in lesions of the cervical spinal cord.

POSTURE AND POSITION OF THE BODY

The posture assumed by the lower extremities is related to the position of the body at rest. Often in supine position the lower extremities are extended; when erect as in sitting, or lying on one side, they are flexed. Thus, in one case, "When lying on one side they [the lower extremities] are usually bent; on the back or stomach, they are straight," or "the usual position of the legs is straightened out when lying [supine] and bent at the knees when sitting"; in another, "Knees [are] partly bent except when lying on back, when straight." Again, "Usual position of the legs is slightly bent when lying down and bent at the knees when sitting."

At times when recovery is taking place, as in the following case, where there was a recovery of sensation on the right thigh, the leg, and the foot and no sensory recovery below the knee of the left side, the legs were extended if the patient was lying supine; if on the right side, the left leg was drawn up, while the right leg was extended. On lying on the left side, the right leg was flexed and the left extended.

What is true of posture is also true of so-called pseudospontaneous spasms. This may be illustrated by a description of one of the patients, who said, "The character of the spasm depends on the position I am in. If lying on side, the thigh and legs tend to draw up and the thighs come together. When lying

† Pollock and associates,[9] p. 550.

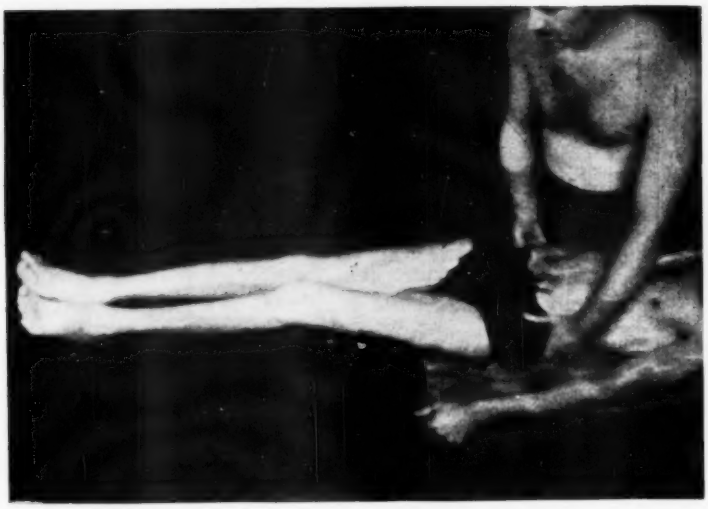


Fig. 1.—Extension of legs when a partially submersed patient, with a spinal cord lesion at T 6, was supine.

on back, the legs tend to straighten out and the thighs cross. If lying on back, the legs tend to straighten out, the thighs come together, the feet turn inward, and the toes come backward and then go into a jerking movement. When lying on side, the thighs and legs tend to draw up and the thighs come together and then relax in several seconds." Another patient said, "Spasm brings the thighs together and straightens the legs stiff, turning the right foot inward. Limbs tremble; muscle draws the legs out stiff; the foot stretches, and the toes turn in a claw-like manner. If sitting in a chair or lying on side with legs in a bent position, the legs cannot be straightened out but draw up." Another patient said, "The spasm draws up and straightens out the legs depending on whether on back or abdomen. Neither occurs first; they alternate, but mostly draw up."

Postural changes were dramatically demonstrated in the case where the patient was partly submerged in water to diminish the retarding effect of friction and gravity. When he was supine, the lower extremities were extended; when the patient was turned to

Fig. 2.—Abrupt flexion of legs of patient in Figure 1 when turned to a side.

a side, there was an immediate and convulsive flexion, and the extremities were again strongly extended when the patient was turned back to a supine position. This is illustrated by the following protocol.

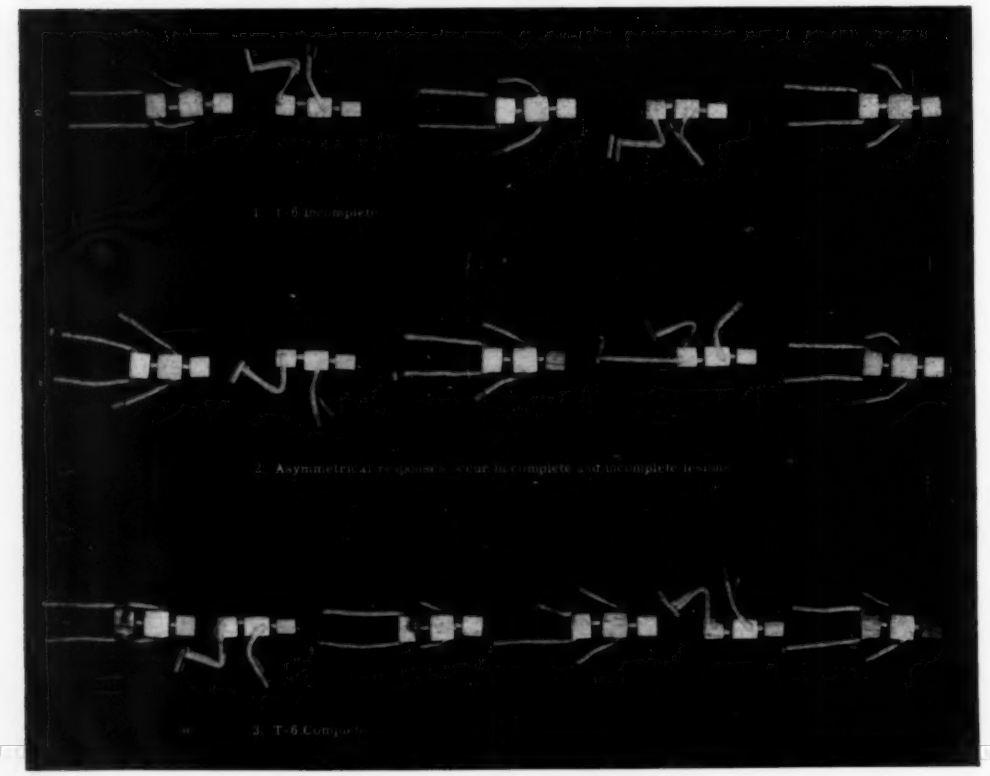
The legs were in extension. Turning the head forward, backward, to the right, or to the left produced no change in the position of the legs. When the patient was supine, the legs were in extension and remained in extension. When turned sharply to the right side, there was immediate flexion of the legs, which again turned into an immediate extension upon the patient's being turned onto the back.

This protocol illustrates the simplest response of bilateral flexion and then extension. It was found in three instances, all of physiologically complete lesions of the thoracic spinal cord (Figs. 1 and 2).

However, asymmetrical responses were observed in 6 of the 16 cases studied—in 5 thoracic lesions, and in 1 cervical lesion. Of the five thoracic lesions, two were physiologically complete and three incomplete. The cervical lesion was physiologically incomplete.

This type of response warrants a description of several cases. The following response occurred in a patient with a physiologically complete lesion of the fifth thoracic segment. When the patient was placed in a supine position the legs were in extension with moderate flexion of the knees. When turned on the right side, there was an acute flexion of the right leg with contralateral extension. When turned on the back, there was a gradual relaxation to a point where the legs were in a moderate flexed position. When he was turned on the left side, there was an acute flexion of both legs. When turned back to the supine position, there was again gradual relaxation of the legs into a semiflexed position.

Fig. 3.—Various responses to change of position, from supine to lateral and back; some symmetrical and some asymmetrical.



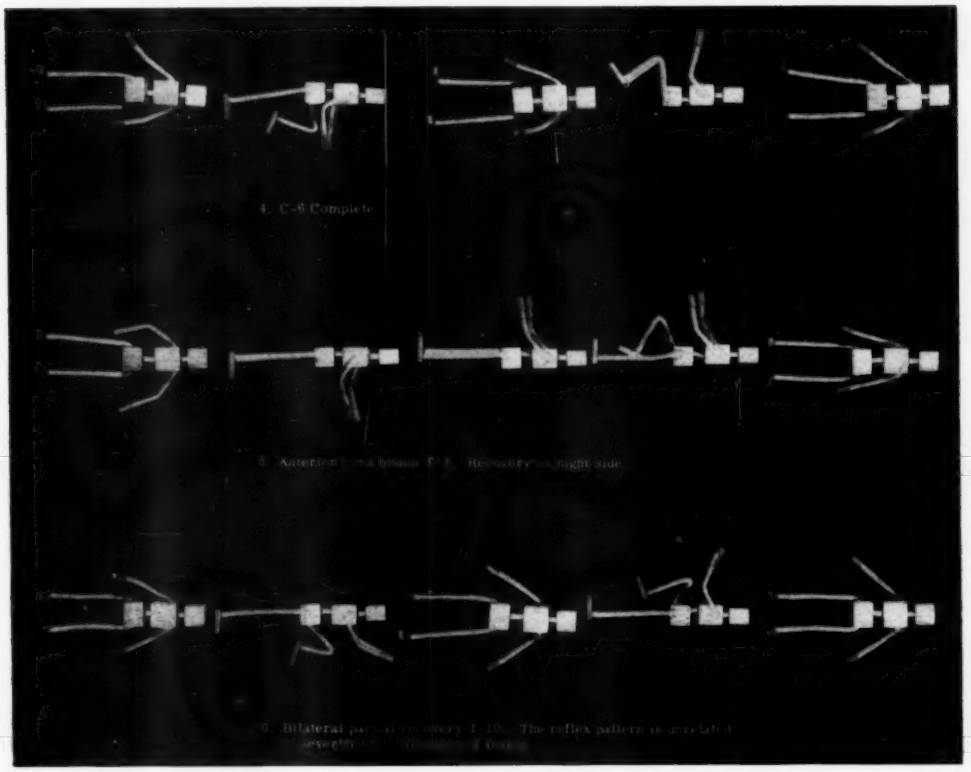


Fig. 4.—Various responses to changes of position, from supine to lateral and back: some symmetrical and some asymmetrical.

In the following case there was a physiologically complete lesion of the sixth thoracic segment of the spinal cord. "The legs were maintained in extension. When turned on the right side there was slight immediate flexion of the right leg with rapid extensor return. There was no accompanying movement of the left leg. When the patient was turned on the right side, an acute flexion of both legs occurred with extension of the legs slowly when placed on the back."

But one more case needs to be described. It is that of a physiologically complete lesion at the third thoracic segment. "When the patient was placed on his back, the legs were extended but slightly flexed at the knees. When he was turned sharply on the left side, there was an acute immediate flexion of the left leg and increased extension of the right. When placed on the back, the legs were extended, with slight flexion at the knees. When placed on the right side, there were an acute flexion of the right leg and increased extension of the left leg. Again, when placed in the supine position, the legs were extended, but were slightly flexed at the knees" (Figs. 3 and 4).

It was found impossible to correlate the pattern of response with the level of the lesion on parts recovering function. This may be understood from a former study (Pollock and associates [9]), where we pointed out that the recovery of function of the distal end of the injured spinal cord consists of an autonomous function peculiar to each spinal cord. For this reason, the responses which we here observe are not necessarily those which are present in normal man and are inhibited at higher levels, only those appearing in a structure developing a new set of activities when, after some time, it develops some function

which is peculiar to each surviving portion of the spinal cord below the level of injury.

This was illustrated, in the above-cited work, by the development of complicated types of pseudospontaneous spasms and successive reflexes.

Responses of some significance were observed in one of four cervical cord lesions, in all of the thoracic lesions (T 1 to T 6 inclusive), and in one of five lesions from T 7 to T 12, inclusive. More consistent responses occurred in the upper thoracic lesions, and less frequently in the cervical lesions. It would appear that the cervical segments of the spinal cord inhibit the release of those body reflexes produced by position of the body. It is expected to find that in the lower thoracic lesions proprioceptive impulses from the trunk must be diminished, or in lowermost lesions absent, thus explaining the absence of those reflexes in such placed lesions.

It is necessary, finally, to indicate that the above-described reflexes were not due to neck or labyrinthine stimuli. This was shown by the fact that in each of the patients the position of the head did not modify the position of the lower extremities.

Moreover, stimulation of labyrinths, although regularly producing marked nystagmus and nausea, also was without effect upon posture of the lower extremities. Abduction of the upper extremities occurred after head turning when the lesion was in the cervical cord with sparing of the fifth segment.

SUMMARY AND CONCLUSIONS

The monumental studies of Sherrington and his school, of Magnus, of de Kleijn, and of Rademaker upon decerebration have laid the foundation upon which studies upon proprioceptive reflexes may be built.

In addition to neck and labyrinthine and righting reflexes from the midbrain, there have been described reflexes arising from changes in position of the body or asymmetrical pressure, some acting on the head and eyes, others on the body itself. We have described the body reflexes acting on the body itself in traumatic injuries of the spinal cord. It has been shown that the posture of such patients varies in respect to their position at rest. A posture of extension is seen when the subject is lying in a supine position, and when the patient was lying on the side, a flexion of the lower extremities is seen.

This relationship between position and reflex response was also described in reference to so-called pseudospontaneous spasms.

Most striking were the reflexes evoked by turning a patient from a supine to a lateral position, back to a supine position, and again to the opposite lateral one. To facilitate the movement, the patients were examined while partly submerged in a swimming pool, to diminish the retarding effect of friction and gravity.

It was found that these reflexes were more readily evoked from patients with lesions in the upper half of the thoracic segments of the spinal cord, less in those with cervical cord lesions, and, of course, slightly or not at all in the lowermost thoracic segments. It was suggested that the cervical spinal cord inhibited reflex activity of the upper thoracic ones. It was natural that the smaller the area from which proprioceptive stimuli entered the spinal cord, the less marked were the reflexes found, and they often were absent.

There was no correlation between the types of recovery, sensory or motor, and the posture assumed by the reflex. Many different patterns were observed. This may be understood if, as we showed before, each distal segment of a severely injured spinal cord develops an autonomous function peculiar to itself and unrelated to that developed in others.

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Digital Vasomotor Responses Following Nerve Root Stimulation

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and
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This study was carried out to determine the presence or absence of vasomotor fibers to the upper extremity in the anterior roots of the upper thoracic and lower cervical roots of man, and to investigate the role of the posterior roots in maintaining vasomotor tone.

Vasoconstriction or vasodilatation may occur in the digits of an extremity following electrical or mechanical stimulation of spinal roots. The digital plethysmograph is especially adaptable to detecting and recording such vasomotor responses.

Plethysmographic recordings were obtained from two digits of the upper extremity of patients during the performance of thoracic anterolateral chordotomy. The operative area was extended to permit stimulation of the upper thoracic and lower cervical posterior and anterior roots.

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From the Departments of Neurological Surgery and Neurology, Columbia University College of Physicians and Surgeons; the Neurological Institute, Presbyterian Hospital, and the Francis Delafield Hospital.

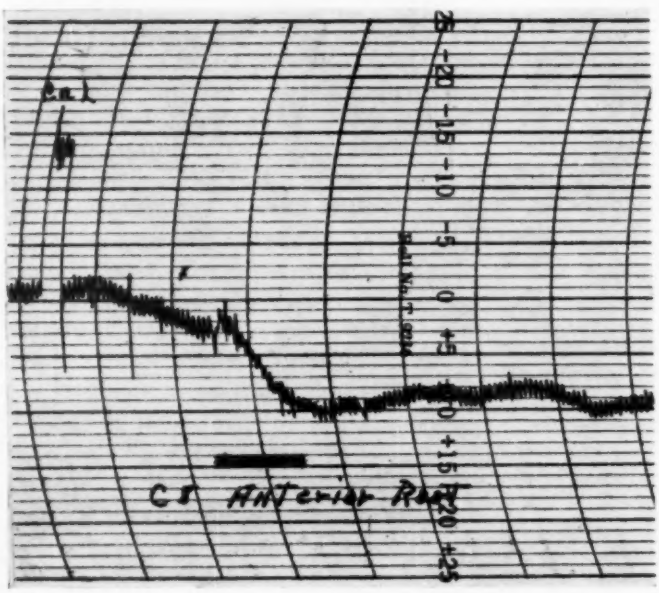


Fig. 1.—Digital vasoconstriction, indicated by reduction of pulse and digit volume, in response to electrical stimulation of the eighth cervical anterior root.

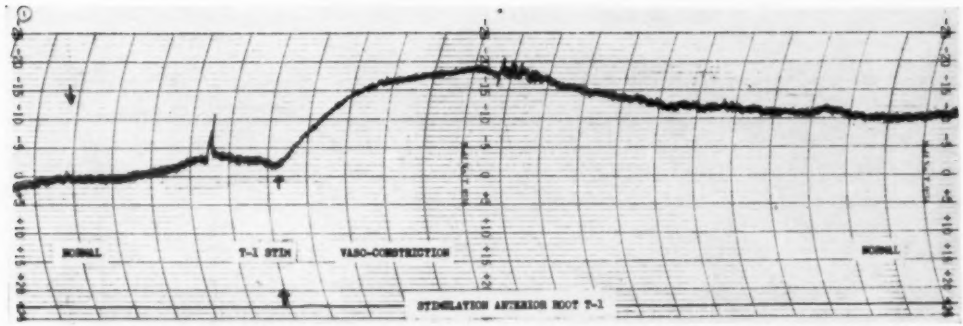


Fig. 2.—Reduction of pulse and digit volume subsequent to stimulation of the first thoracic anterior root. Note that in this record the arrow in left upper corner indicates the direction of increasing volume.

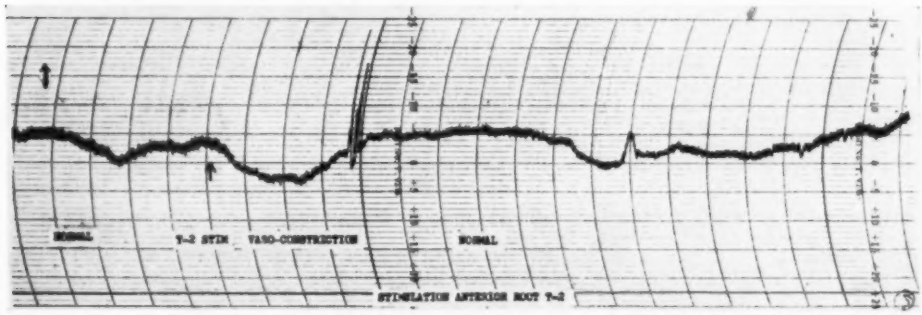


Fig. 3.—Digital vasoconstriction during stimulation of second thoracic anterior root.

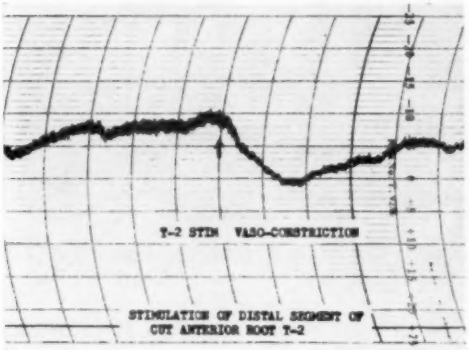


Fig. 4.—Upper: Stimulation of the distal segment of the divided second thoracic anterior root results in digital vasoconstriction.

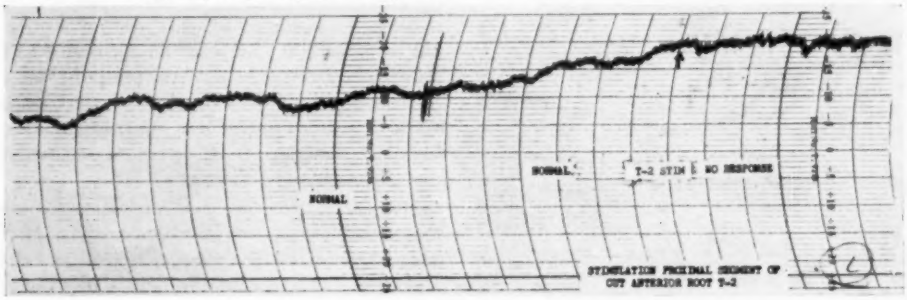
METHOD

The patient was placed on the operating table for cervicothoracic laminectomy. Two digits of one upper extremity or one digit of each upper extremity was sealed within light Celluloid cups by means of printer's roller compound. Each of the two Celluloid cups was connected to a plethysmograph by way of thick-walled rubber tubing.

The plethysmographs were strain-gauge, direct-writing models of high sensitivity.

Posterior and anterior roots of thoracic and cervical origin were identified and stimulated electrically and mechanically. Silver clips were used to "mark" roots for subsequent x-ray confirmation of the foramen of exit.

Lower: Stimulation of the proximal segment of the divided second thoracic anterior root fails to produce a digital plethysmographic response.



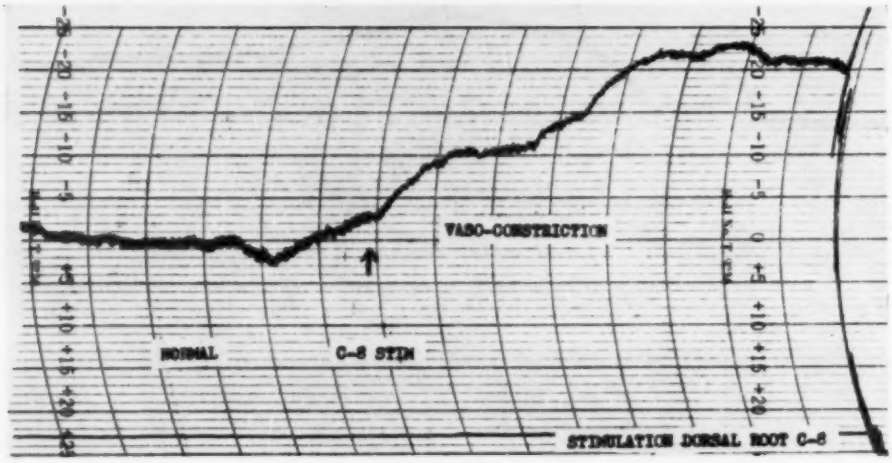


Fig. 5.—Stimulation of intact eighth cervical posterior root produces digital vasoconstriction. In this record decrease of digit volume is recorded by upward deflection of the tracing.

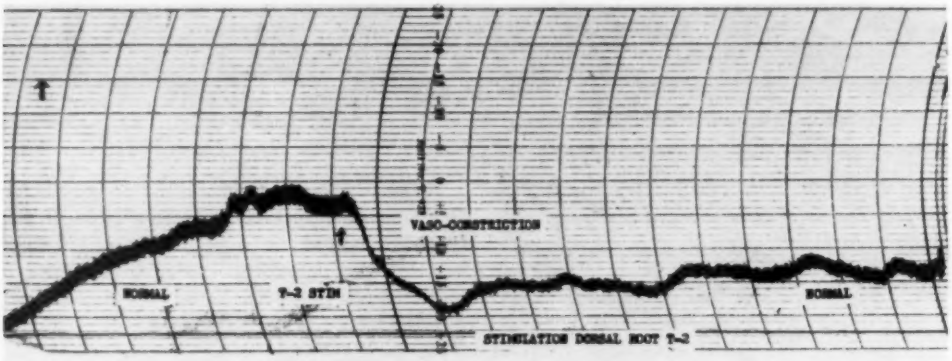
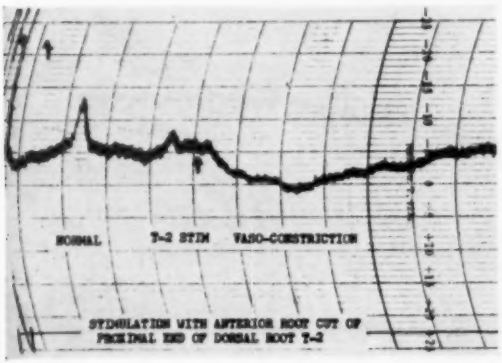


Fig. 6.—Stimulation of intact second thoracic posterior root results in reduction of pulse and digit volume.

Fig. 7.—Vasoconstriction, resulting from stimulation of second thoracic posterior root, is not prevented by section of the corresponding anterior root.



An electrical stimulus strength of 50 to 500 mv. of square- or peak-wave type and a frequency of 200 cps was found to produce consistent vasomotor responses. Responses to stimuli representing lower voltages (50-75 mv.) occurred when stimulating intact roots under local anesthesia. Similar responses required higher voltages (200-500 mv.) when divided roots were stimulated or when general anesthesia was used. General anesthesia did not alter the type of vasomotor responses and was preferred, since it eliminated the patient's restlessness and reduced motor responses to nerve root stimulation. This is especially desirable, since movement of any sort affects the recording system.

After conclusion of the stimulation-recording observation period, the anterolateral chordotomy was performed and the operation brought to a close. There were no untoward effects as a result of this

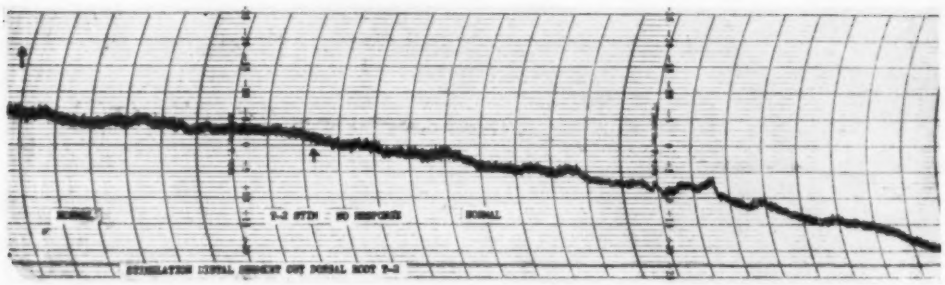


Fig. 8.—Stimulation of the distal segment of the divided second thoracic posterior root fails to produce a plethysmographic response. This indicates that there was no "overflow" of electrical stimulus to the adjacent anterior root or sympathetic trunk.

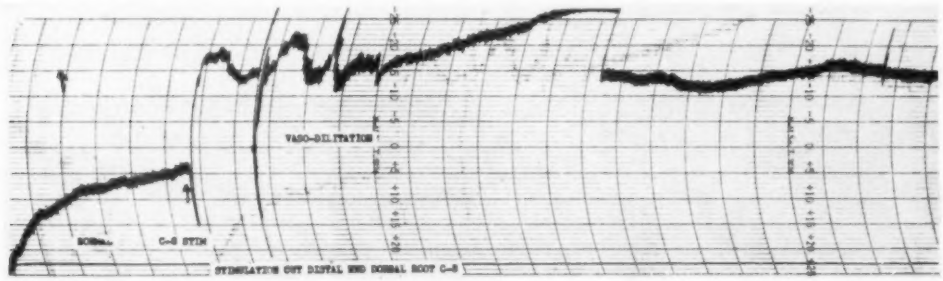


Fig. 9.—Increasing pulse and digit volume (fifth digit) follows crushing and stimulation of the eighth cervical posterior root.

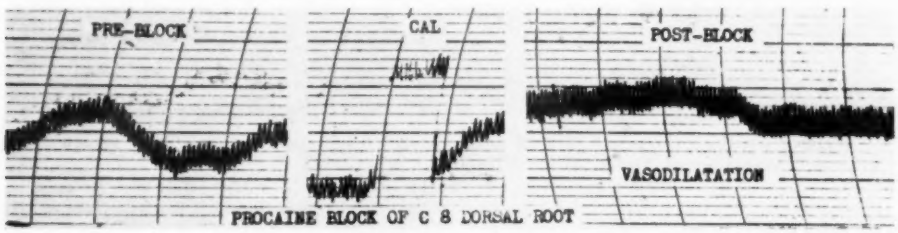


Fig. 10.—Procaine infiltration of the eighth cervical posterior root causes an increase of pulse and digit volume (fifth digit).

study in any of the patients upon whom these observations were attempted or carried out.

RESULTS

Anterior Root Stimulation.—Digital vasoconstriction was produced in digits of the homolateral upper extremity by stimulation of the anterior roots of the eighth cervical and first, second, and third thoracic segments. This digital vasoconstriction involved all digits studied and was never found to be segmental in distribution (Figs. 1, 2, and 3). Stimulation of the distal segment of the divided anterior root resulted in vasoconstriction, similar to that produced by stimulation of the intact root (Fig. 4). Vasoconstriction did not occur in the digits of the homolateral hand following anterior root stimulation.

No vasomotor changes were found to occur in any digit as a consequence of stimulating the proximal segment of the eighth cervical or first, second, or third thoracic divided anterior root (Fig. 5).

Posterior Root Stimulation.—Digital vasoconstriction resulted from stimulation of any intact posterior root from the eighth cervical root through the third thoracic root. The

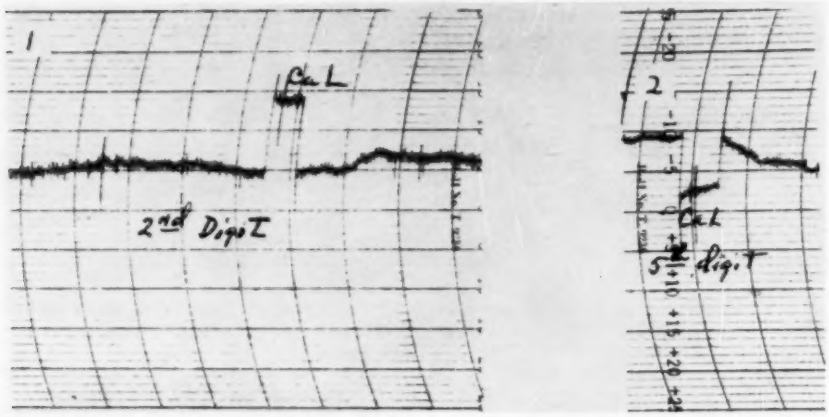
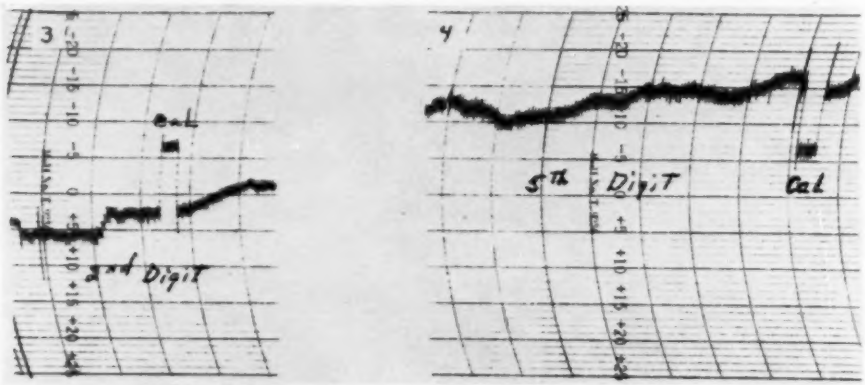
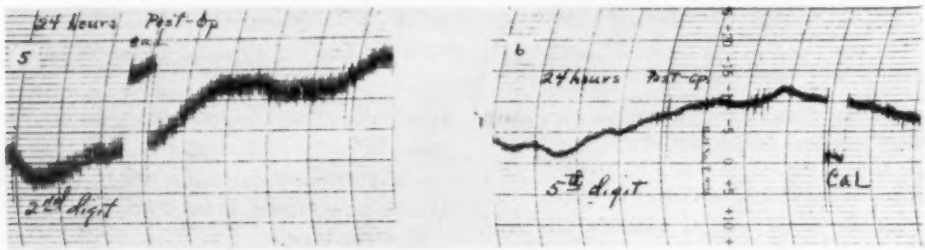


Fig. 11.—Upper: Companion tracings from second and fifth digits of anesthetized patient.



Middle: Crushing the eighth cervical posterior root results in an increase of pulse and digit volume (vasodilatation) limited to the fifth digit.



Lower: Within one and a half hours, vasoconstriction replaced vasodilatation in the fifth digit and persisted for six days. In this tracing, 24 hours after operation, there is a return to a normal, more dilated state in the second digit. This is related to recovery from the anesthetized state.

vasoconstriction occurred in all digits of both upper extremities simultaneously (Figs. 6 and 7).

Vasoconstriction was demonstrated in all digits of both upper extremities during stimulation of the proximal segment of the divided posterior root (C8, T1, T2, T3; Fig. 8).

No vasomotor changes were detected upon stimulation of the distal segment of the

first, second, or third thoracic divided posterior root (Fig. 9).

Vasodilatation and vasoconstriction were elicited after crushing or division of the eighth cervical posterior root. These changes were limited to the fourth and fifth digits of the homolateral upper extremity, which are included in the dermatomic area supplied by the eighth cervical posterior root. Observations were limited to changes following section of the eighth cervical posterior root; no other cervical posterior root was sectioned in any of the patients.

Crushing or cutting of the eighth cervical posterior root initiates vasodilatation in the fourth and fifth digits of the homolateral hand (Fig. 10). The vasodilatation increases over a period of 8 to 10 minutes, is maintained for a period of 30 to 90 minutes, and is then rapidly replaced by intense vasoconstriction, which, like the vasodilatation, is limited to the segment supplied by the crushed or divided posterior root (fourth and fifth digits). This vasoconstricted state persists for 4 to 10 days. With returning sensation within the eighth cervical dermatome, the vasoconstricted state begins to return to normal (Fig. 11).

This vasodilatation, recorded by the plethysmograph, is accompanied by visible flushing and increased skin temperature within the eighth cervical dermatome—the "flare reaction."

The period of vasoconstriction is indicated by pallor and decreased skin temperature, though these phenomena are much less striking than the "flare reaction" of the vasodilatation period.

We have called this phenomenon the "total segmental vasomotor response" to crushing or cutting the posterior root innervating the dermatome in which these vasomotor changes occur.

Stimulation of the distal segment of the divided eighth cervical posterior root on occasion appeared to cause an increase of vasodilatation during the 10-minute interval of increasing vasodilatation, but had no effect after maximum vasodilatation had occurred.

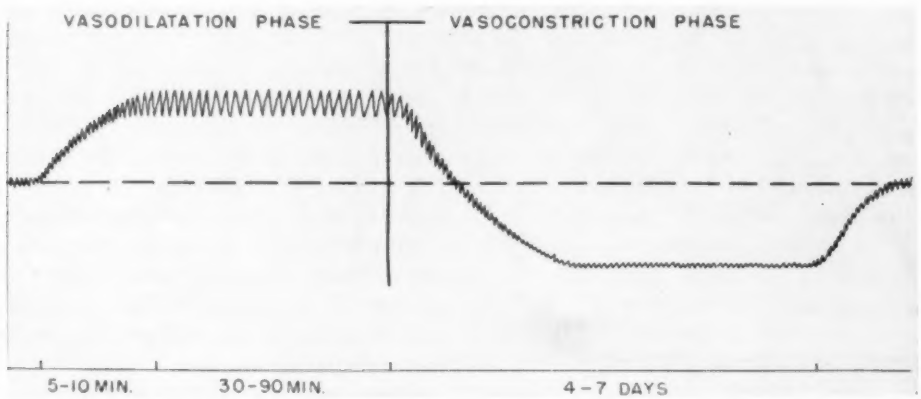


Fig. 12.—Schema of total segmental vasomotor response to section of posterior root.

Inasmuch as section of the eighth cervical posterior root initiated the vasodilatation period, we studied the effect of posterior root block by injecting 0.1 cc. of 4% procaine solution among the fibers of the intact posterior root to interrupt its function. Increase of pulse and digit volume, indicating vasodilatation, occurred after procaine block of the posterior root (Fig. 12). Vasodilatation was confined to the fifth digit. It did not occur in the second digit of the same hand, representing the sixth cervical dermatome, which was used as a control. It was less marked than after crushing or cutting of the root and was not accompanied by flushing of the skin.

Results of posterior and anterior root stimulation are tabulated in the accompanying Table.

COMMENT

The present study was undertaken to determine, if possible, the upper level of pre-

Vasomotor Responses to Posterior and Anterior Nerve Root Stimulation

	No. of Patients	No. of Recordings	Response: Vasoconstriction	Response: Vasodilatation
Intact anterior root				
C8	5	12	+	—
T1	5	14	+	—
T2	6	10	+	—
T3	3	8	+	—
Divided anterior root				
Distal segment				
C8	2	6	+	—
T1	3	6	+	—
T2	3	3	+	—
T3	3	3	+	—
Proximal segment				
C8	2	4	—	—
T1	3	6	—	—
T2	3	6	—	—
T3	3	6	—	—
Intact posterior root				
C8	5	8	+	—
T1	5	5	+	—
T2	6	10	+	—
T3	3	6	+	—
Divided posterior root				
Proximal segment				
C8	3	8	+	—
T1	2	8	+	—
T2	3	6	+	—
T3	1	4	+	—
Distal segment				
C8	5	3	—	+
T1	2	2	—	..
T2	3	5	—	..
T3	1	2	—	..

ganglionic sympathetic innervation to the upper extremity in man and to observe the effects of electrical and mechanical stimulation of posterior roots upon vasomotor tone.

Anterior Root Study. — Foerster [3] observed vasoconstriction of the head and neck following stimulation of the first and second thoracic anterior roots in man, and plethysmographic evidence of vasoconstriction in the arm following stimulation of the third to seventh thoracic anterior roots. He concluded that there is no vasomotor outflow to the arm above the third thoracic segment.

Ray, Hinsey, and Geohegan [8] found decrease in electrical skin resistance of the upper extremity following stimulation of the second thoracic anterior roots (and lower thoracic roots) in 10 patients, but in only 1 patient following stimulation of the first thoracic anterior root, and this occurred on one side only. This work suggested that the uppermost sympathetic outflow to the arm comes from the second thoracic segment.

Surgical sympathectomy of the upper extremity has been more effective in the treatment of hyperhidrosis than of vascular disease, such as Raynaud's.[14] It seemed possible that fibers subserving sudomotor control might be limited to the thoracic anterior roots, as indicated by the study of Ray, Hinsey, and Geohegan. The possibility remained that fibers mediating vasomotor control in the arm may have a more extensive origin, traversing the thoracic and lower cervical anterior roots. If such vasomotor function could be demonstrated in the first thoracic and in the cervical anterior roots, an explanation for the less satisfactory results of sympathectomy for vasoconstriction disorders of the upper extremity would be available.

The anatomical evidence for the presence of sympathetic vasomotor fibers in the first thoracic and the cervical anterior roots was reported by Wrete [15] and Skoog,[12] and later by Kuntz and Alexander.[7] Whether these "by-passing" sympathetic fibers were destined for the head and neck or for the upper extremity, or whether they subserved vasomotor function was not definable on anatomical grounds.

The plethysmographic responses in the digits of the upper extremity following electrical stimulation of the eighth cervical and first thoracic anterior root in five patients revealed vasoconstriction in the homolateral digits. This indicates that the upper

limit of preganglionic outflow to the upper extremity is at least as high as the eighth cervical dermatome.

When this observation is compared with the study of Ray, Hinsey, and Geohegan, which indicated that the most frequent uppermost limit of sudomotor outflow is via the second thoracic anterior root, a reason for the better results of sympathectomy for hyperhidrosis than for vascular disease of the upper extremity is apparent, as the first thoracic and eighth cervical roots are left intact in the usual operation to denervate the arm.

A more important conclusion which may be derived from comparing the two studies is that, while sudomotor and vasomotor functions are both mediated by sympathetic fibers, there are distinct differences in the preganglionic routes of fibers destined to modify sweat-gland and blood-vessel activity. Observations of sympathetic pathways based upon a study of sweat function, e. g., skin resistance, cannot be freely interpreted to indicate a similar pathway for innervation of blood vessels. Sudomotor or vasomotor function each must be measured independently to determine sympathetic activity and to delineate responsible sympathetic pathways.

Posterior Root Study.—The phenomenon of flushing within the dermatomal area supplied by a cut stimulated posterior root was first reported by Strecker, and later studied by Bayliss,[1] Foerster,[4] Hinsey,[5] Westbrook and Tower,[13] and Kahr and Sheehan.[6]

It is believed that we have had the first opportunity to study this "vasodilator phenomenon" in the human quantitatively by use of plethysmograph technique. The recordings indicate that true vasodilatation occurs. It is limited to the dermatomal segment supplied by the posterior root being studied. The "vasodilator phenomenon" is initiated by crushing or sectioning the posterior root. It is not observed with electrical stimulation of the intact root.

It is of great interest that the vasodilatation is only a part of the "total segmental vasomotor response" to posterior root section.

The use of the plethysmographic technique permits observation of the time relationship of stimulus or injury of the posterior root to the development of segmental vasomotor change. As we have indicated, electrical stimulation of the intact root consistently produced vasoconstriction. This began within 1 second of stimulus application and persisted during stimulation, returning to normal vasomotor state within 10 to 20 seconds after stimulation was discontinued.

The vasodilator phase of the "total segmental vasomotor response" begins with cutting or crushing of the posterior root, reaches its maximum in 5 to 10 minutes, and persists at maximum for 30 to 90 minutes, gradually receding, to be replaced by intense segmental vasoconstriction, which will persist for periods of 4 to 7 days (Fig. 12).

The observation that electrical stimulation of the intact root produced vasoconstriction and that, following section of the posterior root, there was no increase in vasodilatation with electrical stimulation, once vasodilatation had reached its maximum, led to the study of the vosomotor response to posterior root interruption by procainizing it. When the posterior root is procainized, segmental vasodilatation occurs. This can be demonstrated plethysmographically, though a skin flare could not be detected. The period of vasodilatation was followed by a return to "normal" pulse and digit volume.

While these observations do not establish the presence or absence of vasodilator posterior root efferent fibers, they do suggest that the integrity of the posterior root is essential for the maintenance of segmental vasomotor control. It may be that interruption of the sensory limb of a segmental vasomotor reflex arc leads to the altered vasomotor state reflected in the "total segmental vasomotor response." If this is the case, the vasodilator component represents a period of paralysis of segmental vasoconstriction activity, and the subsequent,

and much longer, vasoconstriction period indicates a long period of unmodified, or excessive, vasoconstrictor activity.

Failure to produce vasodilatation or vasoconstriction by crushing or stimulating the divided posterior root occurred in two out of five patients. In one such instance no change in digital vasomotor tone could be demonstrated, and while the eighth cervical dermatone could be identified as an area of impairment, loss was minimal and limited to impairment of light touch and two-point discrimination. Pinprick could be perceived and localized, and temperature sense was well preserved.

SUMMARY

It has been found possible to obtain good evidence of vasomotor phenomena occurring within digits of the upper extremity following stimulation of the lower cervical and upper thoracic nerve roots by means of the direct-writing, strain-gauge type of digital pneumoplethysmograph.

Plethysmographic tracings show that vasoconstriction occurs in the digits of the homolateral extremity following electrical stimulation of the eighth cervical and first, second, and third thoracic anterior roots and indicate that preganglionic sympathetic fibers carrying vasomotor impulses to the digits of the upper extremity exist within these four roots.

Decrease in pulse and digit volume, indicating vasoconstriction, has been found to be a constant result of electrical stimulation of the intact lower cervical or upper three thoracic posterior roots or of the stimulation of the proximal segment of any one of these roots. The vasoconstriction response occurs bilaterally. It is mediated through the cord. Furthermore, this "posterior root vasoconstrictor response" has been found to be of value as a means of determining the minimal electrical stimulus required to produce vasomotor responses by stimulation of either posterior or anterior roots in the individual patient.

Segmental dilatation has been shown to occur after division of a posterior root supplying the dermatome under observation, and this vasodilatation has been recorded plethysmographically. The use of the plethysmograph has permitted observations to be made upon the gradual development of this vasodilatation over a period of 5 to 10 minutes; its duration, of from 30 to 90 minutes, and its gradual subsidence, to be replaced by marked vasoconstriction, lasting from 4 to 7 days. This complete phenomenon of vasodilatation followed by vasoconstriction has been termed the "total segmental vasomotor response."

It has been found that vasodilatation within the dermatomes supplied by the eighth cervical posterior root may be elicited by crushing, by cutting, and by procainizing the posterior root.

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News and Comment

ANNOUNCEMENTS

Israel S. Wechsler Lecture.—The first Israel S. Wechsler lecture is to be given on the evening of Dec. 2, 1955, at the Mount Sinai Hospital of New York by Dr. John F. Fulton, Sterling Professor of the History of Medicine, Yale University School of Medicine.

GENERAL NEWS

Congress of Neurological Surgeons.—The Congress of Neurological Surgeons held its annual meeting in Los Angeles at the Statler Hotel from Oct. 26 to Oct. 28.

Association for Research in Nervous and Mental Disease.—The 35th Annual Meeting of the Association for Research in Nervous and Mental Diseases will be held on Dec. 9, and 10, 1955, at the Hotel Roosevelt, New York. The subject of the meeting will be "The Neurologic and Psychiatric Aspects of the Disorders of Aging."

Communications may be addressed to Clarence C. Hare, M.D., Secretary-Treasurer

American League Against Epilepsy.—The annual meeting of the American League Against Epilepsy will be held at the Hotel Roosevelt, New York, Dec. 8, 1955.

Association for Clinical and Research Studies of the Ypsilanti State Hospital.—The Association will hold the following seminars at the Ypsilanti State Hospital, Ypsilanti, Mich.:

Nov. 18, 1955: Direct Analytic Treatment of Schizophrenia, Dr. John N. Rosen

Jan. 20, 1956: Integration of Cultural, Anthropological, and Social Sciences with the Problems of Mental Health, Dr. Margaret Mead, Ph.D.

March 23, 1956: New Perspectives in Public Psychiatry, Dr. George S. Stevenson

Further information may be obtained from Dr. Richard B. Hicks, Ypsilanti State Hospital, Ypsilanti, Mich.

A Mechanism in Schizophrenia

A Theoretical Formulation

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Ever since dementia praecox was first described by Kraepelin numerous theories have been proposed to explain its pathogenic mechanisms. These theories have varied widely in their conceptions and approach, but as yet no completely satisfactory solution to the problem has been found. Certainly the often-repeated and too-often-taught formulation, that schizophrenia represents a defensive withdrawal from reality in order to avoid the anxiety arising from the patient's neurotic conflicts, leaves something to be desired. For to consider schizophrenia as akin to severe neurosis fails to convey what every psychiatrist must at some time have perceived in his patients: their feelings of chaotic experience, of utter helplessness, of being unable to control their reactions or carry out intention, the feeling of having undergone some terrible, indescribable alteration which reaches somehow into the depths of the personality.

The impression that schizophrenics experience an inner dissolution of their integrative capacities leads one naturally to question the idea of a dynamic purposefulness of this aspect of the illness. There are both quantitative and qualitative differences between this schizophrenic disorganization and the specific defense mechanisms of the obsessive-compulsive or phobic patients. Regardless of the presence or absence of symptoms obviously arising from unconscious conflictual material, there is always a substratum which seems to reflect a loss of capacity for functioning that differentiates the schizophrenic from the neurotic.

It would seem desirable, therefore, that a formulation be presented, derived from clinical observations, which takes these factors into account. Such observations are by no means unique, and are familiar to every experienced psychiatrist. The most comprehensive description of the clinical manifestations is still that of Bleuler,[2] who points in particular to two so-called "primary" disturbances in schizophrenia, i. e., disturbances of associations and disharmony of affect. These he considers the "simple," or basic, functions which are deranged by the disease.

If we accept Bleuler's evaluation, it is possible to develop a logical theory which would be subject to examination and proof. Such a theory, briefly stated, might be as follows:

If in schizophrenia associations are disorganized and affect is separated from idea, then in the normal these functions must be organized and integrated. We are led, then, to postulate some mechanism that serves to organize and to integrate these functions in the normal, the disturbance of which will result in the manifestations of schizophrenia.

If such a mechanism exists, it would most probably operate according to principles already established for maintaining the organization of the other body functions, rather than according to new or alien principles. Such a principle would be that of homeostasis, according to which an internal regulation is maintained in the various somatic activities, allowing for adaptation to stresses and stimuli of various sorts. In this event, we might expect a homeostatic mechanism for regulation of mental func-

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tions to be analogous to, and probably associated with, the central homeostatic apparatus for the body as a whole, i. e., the hypothalamic-endocrine axis.

If our assumptions are correct, there should thus be some anatomophysiologic mechanism arising in the diencephalon and projecting to the higher cortical centers to subserve these integrative and regulatory functions.

Reasoning again from the cardinal symptoms of schizophrenia, we may consider that these regulatory activities must be of at least two types, representing a reversal or correction of the disturbances found in schizophrenia. The first of these, which we may call selective conation, would be responsible for the focusing of conscious attention upon a single thought or idea at a time, resulting in an orderly progression of significant associations. The second form of activity would serve to relate idea and affect in a harmonious manner, and we may refer to this as emotional association.

The principle of emotional association suggests that affect and idea represent two functionally independent systems which are somehow integrated to operate harmoniously. These systems may be thought of operationally as an ideational, or associational, unit, and an affective, or emotional, unit. In turn, there is implied a dependence between the two units on the basis of the common mechanism for their integration.

While such speculations represent a decided oversimplification of the problem, their substantiation would allow us to establish a working concept of schizophrenia which could serve as an orientation for future research. Such substantiation should give evidence (*a*) to demonstrate that schizophrenia represents a disturbance of homeostasis involving the biological unit; (*b*) to delineate an ideational and affective "unit," and (*c*) demonstrate an operational mechanism which might serve to integrate the two "units."

A review of the literature reveals evidence from many sources that tends to support these speculations.

SCHIZOPHRENIA—A HOMEOSTATIC DISTURBANCE

Schizophrenia is generally regarded primarily as a "mental" disorder. However, the fact that most cases manifest somatic disturbances, as well as mental abnormalities, has long been recognized and has commanded the attention of many investigators. Most physiologic studies done on schizophrenic patients have attempted to discern possible etiological factors. A number of authors, however, have noted a relationship among the specific findings, diverse or incongruent as they may seem. This evidence, viewed as a whole, strongly suggests that these widespread pathological findings represent different aspects of the same process, namely, a disturbance of the homeostatic equilibrium.

Just about every aspect of function has been studied. For purposes of evaluating the homeostatic mechanisms, these studies may be divided into two groups: those which investigate metabolic activity or blood constituents normally kept constant by homeostasis, and those which measure the capacity of the homeostatic defenses to restore equilibrium after the patient has been subjected to a stress.

With regard to the first group, Bellak [1] reports that studies on circulation and blood constituents revealed a greater variability of findings than occurs in normals, with a greater percentage of abnormal findings but no consistent trends. With regard to carbohydrate metabolism, he reports that here, too, is found a greater variability than is seen in the normal, with the consistent finding of an abnormal glucose tolerance curve with states of tension. The most significant finding in cerebrospinal fluid studies reported by him appears to be an increase in albumin, found by some workers. Studies of the spinal fluid by later workers [15] indicate quantitative differences in the spinal fluid iron content between acute schizophrenics and deteriorated patients. "The high iron values of the deteriorated group seem to reflect a general lowering of oxidative processes in these patients with far-advanced schizophrenia."

Endocrine studies have also been done. Bellak [1] reports that several workers have found gonad atrophy on biopsy of the testis in some cases. Variable thyroid abnormalities have been described. Bowman and his group, at the Langley Clinic,[3] found that schizophrenics have a significantly lower basal metabolic rate than have controls. Hill [10] reports that a number of studies indicate a greatly increased tolerance to thyroid in schizophrenic patients.

Much study has been done on the EEG pattern in schizophrenia. According to Bellak,[1] most workers found that there were more abnormal and borderline tracings in schizophrenics than in controls, but there was no consistent or diagnostic pattern. Some workers found a similarity between the records of patients with psychomotor seizures and those of schizophrenics, and others reported a lack of responsivity to stimulation of the hypothalamus.

We may summarize the results of all these studies, as well as of others on such metabolic functions as body temperature, blood pressure, and heart rate, in the words of Hoskins,[12] who comments that "the average variability in schizophrenia ranges from almost one and one-half to twice more than in normal persons of similar ages."

Responsiveness to stress has received exhaustive study, particularly in recent years. Bellak [1] reports findings of a general reduction of physiologic responsiveness by a number of workers. Much attention has been centered on the pituitary-adrenal mechanism. The group at Worcester State Hospital, studying adrenal responsivity in schizophrenics and in normals under various conditions of stress * found such responsivity, as indicated by a number of methods, noticeably decreased. These results were substantiated in part by some workers,† while others [6] obtained equivocal results. The Creedmoor Group,‡ on the other hand, noting that such therapies for schizophrenia as insulin coma and electroshock, as well as their own histamine therapy, exert an effect over a period of time "which is antiadrenal in some respects," postulated an adrenocortical excess associated with schizophrenia.

Lindsay,[16] reviewing the many physiologic and biochemical studies done in catatonic schizophrenia, concludes that the evidence points to a defective homeostatic mechanism in this disorder and believes that the source of this defect lies within the central nervous system. This conclusion is in close agreement with that of Hill and his group, who, after extensive investigation of the homeostatic defenses, postulate a defective "central homeostatic mechanism in schizophrenia," the integration and organization of which are believed to lie in the hypothalamus.

AFFECTIVE AND IDEATIONAL "UNITS" OF THE BRAIN

Intellectual functions have long been ascribed to the cerebral cortex, and the literature is far too extensive for review here. Halstead's volume,[8] as well as the earlier monograph by Brickner,[4] present detailed discussions of these functions of the brain. We may state, however, that, as the result of careful investigations, the anterior frontal "association areas" are no longer regarded as silent, but, instead, have most frequently been described as centers of intellectual activity. Specific functions ascribed to these areas are the ability to abstract, the ability to plan, and social judgment. Halstead [7] regards the frontal lobes as the seat of "biological intelligence" and proposes a four-factor theory to include these functions in a unitary concept. He concludes:

> Biological intelligence is a basic function of the brain and is essential for many forms of behavior. . . . While it is represented throughout the cerebral cortex . . . it is distributed in a gradient with its maximal representation occurring in the cortex of the frontal lobes. . . . At least some of the factors which are essential for ego formation and growth have their maximal representation in the anterior portions of the frontal lobes of the brain.

It is only comparatively recently that the function of affective experience has been

* References 5, 11, 24, and 28.

† References 10 and 19.

‡ References 26 and 27.

given a localization comparable to that of the intellect. One of the earliest significant observations was made by Hughlings Jackson, in 1899, who found the emotional experience of déjà vu to be associated with lesions of the hippocampal gyrus of the temporal lobe.§ Jackson's observations remained uninterpreted until Herrick,[9] in 1944, on the basis of comparative studies, suggested that the rhinencephalon, in addition to mediating the sense of smell, serves as a nonspecific activator for all cortical activities, influencing appropriately, in an excitatory or inhibitory capacity, such functions as memory, learning, and affective behavior.

It was Papez,[20] however, in 1937, who first proposed that the archipallial structures might be looked upon as the mediators of emotional experience. Since that time, experimental and clinical investigation has lent increasing support to Papez' idea, and has broadened the concept as well.

In 1939 Klüver and Bucy found that severing the limbic structures during bilateral temporal lobectomy transformed wild, ferocious monkeys into docile animals. Further, it was noted that these animals exhibited an oral behavior resembling that of the human infant, examining all objects with the mouth. The association of oral activity with temporal lobe lesions involving the limbic system has also been seen in humans. Cases of voracious appetite, with an apparent inability to stop eating, have been reported by MacLean.[17] Vocalization was also noted by this author. These findings led him to suggest that the limbic portion of the frontotemporal region appears to be organized around the oral activities of the animal as they pertain to feeding and to the vocalization, attack, and defense involved in obtaining food.

Further evidence pointing to the effective function of the rhinencephalon came from studies linking the limbic lobe with autonomic and visceral activity. Papez demonstrated fibers from the ventromedial nucleus of the thalamus, believed to receive visceral impulses, which passed into the amygdaloid nucleus, suggesting that the amygdala may be a visceral-olfactory correlation center.[17] Many workers have described emotional reactions associated with visceral sensations in patients with temporal lobe lesions involving the limbic structures. Thus, patients would speak of a "sick feeling" in the stomach, mouth, or throat; a "nervous feeling" in the stomach which rose to the throat and became a "taste"; a "familiar feeling" associated with epigastric sensation; a "lousy feeling" in the stomach, etc. Penfield and Jasper [22] have also reported cases in which patients described emotions, such as loneliness or fear of sadness, which were felt to be localized beneath the sternum. MacLean [17] reports a patient who related a feeling of sadness to his epigastrium, and another who referred to his epigastrium the feeling of wanting somebody near him. MacLean considers the epigastric aura and its associated sensations to represent raw, poorly differentiated, and impersonalized feelings.

Commenting on the primitive cytoarchitecture of the cortex of the limbic lobe, MacLean continues [17]:

> Considering the affinities of the limbic cortex generally to the type that mediates the sense of smell, can one infer that the limbic system as a whole likewise interprets experience in terms of quality and intensity? This could account perhaps for the varying intensities and qualities of experience that are

§ The hippocampal gyrus is an archipallial structure and forms a part of what Broca described as the "limbic lobe" because of its distribution around the medial surface of the cerebral hemispheres. The structures included by Broca were the cortex adjacent to the olfactory striae; the pyriform area; the hippocampal gyrus and hippocampus, and the parasplenial, cingulate, and subcallosal gyri. Because of the olfactory functions of some of these structures, the entire area was renamed the "rhinencephalon" by Turner, and it was long assumed to be the "smell center" of the brain.

The limbic lobe can now be defined cytoarchitecturally as archipallium and mesopallium. It would include, in addition to the structures grouped by Broca, the architecturally similar insula and temporal polar gyrus. Yakovlev includes the cortex of the orbitomesial surface of the frontal lobe as well. Nuclear structures associated with the limbic system include the amygdala, septal nuclei, hypothalamus, epithalamus, anterior thalamic nuclei, and parts of the basal ganglia.

associated with emotional feeling. Phylogenetically, it is not until the great elaboration of the supragranular layers in the cortex associated with the senses of sight, hearing, and touch, that one finds the development of the kind of cognition that can deal coldly, analytically, and abstractly in terms of symbolic language. . . . Evidence is gradually accumulating that the various internal and external senses are represented in the limbic system. . . . As a working hypothesis, it can be inferred that the limbic system is for the "body viscus" a visceral brain that interprets and gives expression to its incoming information in terms of *feeling*, being incapable perhaps of getting at the meaning of things at the level of symbolic language. . . . In the frontotemporal portion of the limbic system there is growing evidence that the memories and feelings related to the "oral" senses are partially integrated and tied into the workings of the brain as a whole.

A CENTRAL INTEGRATION MECHANISM

Penfield [22] has stated that "anatomical relationship suggests a particularly close association of the anterior, frontal and limbic cortex with the centrencephalic integrating system." The word "centrencephalic" was coined by Penfield [21] to refer to "that system within diencephalon, mesencephalon and probably rhombencephalon which has bilateral functional connections with both cerebral hemispheres." Such a system was described by Magoun [18] and his co-workers, in 1949, on the basis of stimulation experiments. They distinguished two functional elements within the central reticular formation of the brain stem, particularly in the midbrain and diencephalon. The first of these elements, laterally placed, carried the traditionally recognized specific sensory afferent paths. The second, more medially located, was described as a series of ascending relays which function to maintain the waking state. Other workers [25] substantiated these findings and delineated the projections of the ascending reticular system to the cortex.

Jasper and his co-workers [13] demonstrated that this system not only acted as a "center of consciousness" but also had an influence in maintaining the pattern of electrical activity of the cortex. Rose [25] demonstrated that this system projected to the cortex in a diffuse manner, as compared with the specific localized projections from the ascending sensory systems.

Jasper [13] further demonstrated that, while the specific and diffuse systems were independent, there was a functional interaction between them mediated by way of a feedback circuit. He concludes that the diffuse system is responsible for the secondary elaborations of impulses reaching the cortex via the specific systems and that it exerts "a regulatory or integrating effect on these elaborations."

FORMULATION

In order better to understand the operation of these mechanisms and principles, let us view man as an adaptive organism operating according to the principle of homeostasis; i. e., a stress, internal or external, results in compensatory activity by the organism that tends to offset the stress and restore equilibrium. In addition to stresses from without, the organism is subjected to stresses from within, arising from the continued functioning of parts of itself, so that, for example, the emptying of the stomach creates a stress that is offset by filling it again, while the full stomach creates a stress which is offset by emptying it. In this way there are repeated cycles and continuous activity, shifting the equilibrium first this way and then that, with resultant dynamic activity. A static equilibrium is reached only with death.

This homeostatic activity, then, is responsible for the maintenance of life in the organism, insuring its continued existence by promoting the functions of nutrition, metabolism, reproduction, and even defense against attack. In any complex organism homeostasis is maintained in a number of ways and at a number of levels. Thus, the comparatively simple adjustment to an alteration of environmental temperature of only a few degrees affects the functioning of the respiratory system, the blood constituents, the cardiovascular system, etc., and alters somatic behavior at such diverse levels as intracellular oxidation (chemical) and muscular activity (kinetic).

Such a complex adaptive organism requires a similarly complex system of communica-

tion, whereby stimuli and responses occurring in widely separate parts of the organism and at different energy levels may be coordinated and integrated to subserve the adaptive functioning of the organism as a whole.

This coordination is made possible by a system of message-carrying connectors transmitting information to and from a central switching organ, which routes these messages along appropriate paths. In organisms as complex as man, this switching or routing of messages cannot be left to chance, nor can built-in circuits be relied upon entirely for effective functioning. A great freedom of choice is necessary to allow for flexibility in adaptation to unusual circumstances. Problem solving is a commonplace necessity for man's adaptation to his ever-changing environment and his successful survival.

Man's internal environment is handled rather simply. The internally arising stimuli are either offset reflexly at the local level or transmitted to the central mechanism in the hypothalamus and pituitary, where peripheral alterations are effected via the endocrine or autonomic nervous system. These mechanisms are simple enough to operate at an almost reflex level, below awareness.

Man's external environment is not so easily handled. For instance, a message arising in the stomach must be recognized as a need for food, and this recognition must then be translated into effective behavior to offset the stress and restore homeostasis. This could be done with built-in tropisms in simpler forms, but the increased complexity of the organism is accompanied by increased complexity of its needs, and a capacity for greater differentiation between objects in the environment soon becomes necessary. A crude thalamic consciousness was present in early forms to provide them with a protopathic awareness of their contacts with the environment. In the vertebrates an emotional, or visceral, consciousness seems to enter the picture as well. The primitive vertebrates "follow their noses" in obtaining visceral satisfactions, acquiring food, etc. This is more than a tropism, for there is now reason to believe that the rhinencephalon, or "smell brain," is a center of emotional apperception as well. The smell impulses, unlike the other incoming messages from the external environment, are not transmitted to the thalamus, but apparently are translated to awareness at an emotional level within the archipallium.[17] It is likely that attempts to relieve the stresses or "drives" arising from the internal environment were early governed by these emotional responses to various olfactory stimuli arising from objects in the environment. This approach would apply to much vital behavior, including mating as well as feeding. It appears likewise reasonable that, with increasing complexity of the organism, progressive development of the "switching" or integrating organ led to a decreased importance for olfactory stimuli, with an increasing importance for somesthetic, auditory, and visual stimuli, and a consequent representation of these messages as "feelings" in the emotional sense. This may have been the story of the development of the mesopallium.

Logically, it would seem that the central nervous activity of such a mesopallial animal [22] could be considered as follows: The visceral consciousness, by virtue of an emotional awareness, serves to forecast the success or failure of a particular environmental object in satisfying the inner needs. But, also, visual, auditory, and somesthetic imagery projected from the thalamus to the limbic cortex has become capable of conditioning an associated emotional response from the contiguous archipallium. Now, predictions can be made of the potential success or failure of a proposed behavioral activity in satisfying the organism's adaptational needs. The "proper" pattern of behavior is chosen on the basis of the most "favorable" emotional response and is translated into activity, perhaps via the basal nuclei.

The development of the neocortex allowed for much more flexibility. One of the most important advances was the elaboration of a rational consciousness (as distinct from the strictly emotional consciousness), which allowed the organism to deal with abstract symbols and greatly expanded the adapta-

tional success. This "intellect" allowed for greater accuracy of differentiation and for more highly productive synthesis (middle level of integration of Penfield).

But even as the receptor and effector centers moved upward, superseding their more primitive counterparts as primary determinants of behavior, they remained in communication with each other and with the archipallium by way of the centrencephalic system (highest level of integration of Penfield).

We may venture that the limbic, or rhinencephalic, cortex exerted a regulatory effect on percept-concept-idea elaboration. The relationship appears to be essential and reciprocal, and mediated by way of the feedback circuits of the nonspecific projection systems. This mechanism, with its integrative and organizing functions, could make up the essence of what we have come to regard as the ego. The neocortex, with its 1- and 2-degree elaborations of perceptions and complex association pathways, may well operate at a high level of abstraction as a differential analyzer of the digital type.[29] The frontal lobes may constitute a sort of "grand totalizer," with a progressive reduction in the influences of emotional factors as higher levels of abstraction are reached. These are the highly ratiocinative functions, such as calculations and intellectual judgment, which may constitute several areas of Halstead's "biological intelligence"[7] and may represent the portion of the ego which is said to remain "intact" in schizophrenia.

The brain thus seems to function in the mental sphere as a mechanism which analyzes and interprets incoming stimuli in terms of past experience and inherent neuronal patterns, serving to predict for the individual the relative effectiveness of proposed behavior in adapting to internal and external needs and stresses. These predictions may be conscious and rational, perceived as logical deductions; or they may be emotional, perceived as pleasant or unpleasant feelings.

In individual maturational development we may expect a series of events quite similar to what we postulated phylogenetically. We may consider that the adaptive behavior of the newborn infant operates at a reflex level.[23] Shortly thereafter, rhinencephalic mechanisms may be seen, as the infant attends first to inner (visceral) needs and makes his contacts with the outside world by mouthing. This oral behavior may herald the onset of the development of primitive "thinking" (what Freud called the primary process), which takes the form of imagery, coupled closely with affective experience. Resulting behavior first rejects, then avoids, those stimuli whose percepts are associated with unpleasant affects. Soon there develops the capacity to differentiate between the environmental stimuli transmitted via nonvisceral receptor pathways, and the infant is noted to look, listen, and touch as often as he mouths.[23] His attention is held first by small details; later he can synthesize these delimited stimuli, and responds to entire objects in his environment. His "thinking" now, still at the primitive "imagery-emotion" or (archipallial) stage, allows him to relate to objects in his environment according to the affect engendered by the total percept. The poles of affective experience now may be described as security *vs.* anxiety. However, he is as yet unable to distinguish between internal and external stimuli and apparently regards the environment as an extension of himself, as he appears to employ the same techniques for mastering it as for mastering his own body. This seems to be due to the fact that his operational level is still emotional, so that, although he is able to differentiate percepts on the basis of affective experience, he cannot identify or correlate them.

Apparently, it is not until the neocortex assumes dominance that ego differentiation can begin. Incoming stimuli, while still provoking the usual affective responses at the archipallial level, are now transmitted to the new cortex, where receptor centers for auditory, visual, and somesthetic modalities allow for more exact definition of percepts. Areas contiguous to these receptor centers make possible elaborations of these stimuli, so that incoming messages may be classified and distinctions drawn between members of the

same class. Now percepts may be recognized as members of a group or as specific entities, whereas at the more primitive level all objects of the same class were treated similarly, or else the generic relationship was overlooked. In addition, by a secondary elaboration, individual, as well as class, percepts may be recalled, thus adding immeasurably to the predictive efficiency of adaptive behavior.

A higher level of analysis is possible through the intercommunication of these receptor and elaborative centers by way of the multitude of associational pathways. This allows for the correlation of information from all the sensory modalities and results in a dimensionally oriented concept formation.

It would appear that only those stimuli transmitted by the exteroceptive apparatus undergo such neocortical elaboration. Enteroceptive stimuli continue to be dealt with in the archipallium, or limbic system (including the insula). The differences between the apperceptive qualities of the two systems provide the basis for the distinction of source of stimuli, i. e., internal and external, and allow for the differentiation of a concept of self as distinct from environment. The establishment of the "ego boundaries" may be heralded by a negativism the purpose of which may be to intensify and delimit more sharply and clearly the "I" from the "not I"[14]: At times, too, there may be noted a new demanding and autocratic type of behavior, which may represent a reluctance to accept this differentiation, a refusal to part with an environment which was formerly perceived as an extension of the self.

With the development of language, the child's thought processes assume a new dimension. Verbal speech seems to depend on the ability to differentiate sound in a highly specific way (plus the capacity for motor reproduction of these sounds), together with the development of an associational relationship between the given sound and a specific concept. As language develops, the words may be used in place of the concept, and thinking in terms of "imagery" is no longer essential. It now becomes possible to utilize *ideas* as a more precise, though slower, method of facilitating predictive behavior, allowing for long-term planning, social judgment, etc. These "ideas" may themselves serve as stimuli, and logical abstractions may be made without direct reference to percepts (secondary process).

It would seem, however, that a relationship continues to operate between the newer and the older brain which apparently serves two major purposes with regard to adaptive behavior: On the one hand, it permits information regarding inner needs (enteroceptive stimuli, "instinctive drives") to reach neocortical awareness and to be dealt with more efficiently on an ideational level. On the other hand, it allows for a cross check (with the frontal lobes) of the predictive behavior at the ideational level; i. e., it regulates or guides ideational activity away from anxiety-provoking patterns.

This relationship is thus reciprocal, and the evidence seems to indicate that the centrencephalic system provides this relationship through its feedback circuits. This mechanism appears to represent the principle of emotional associations.

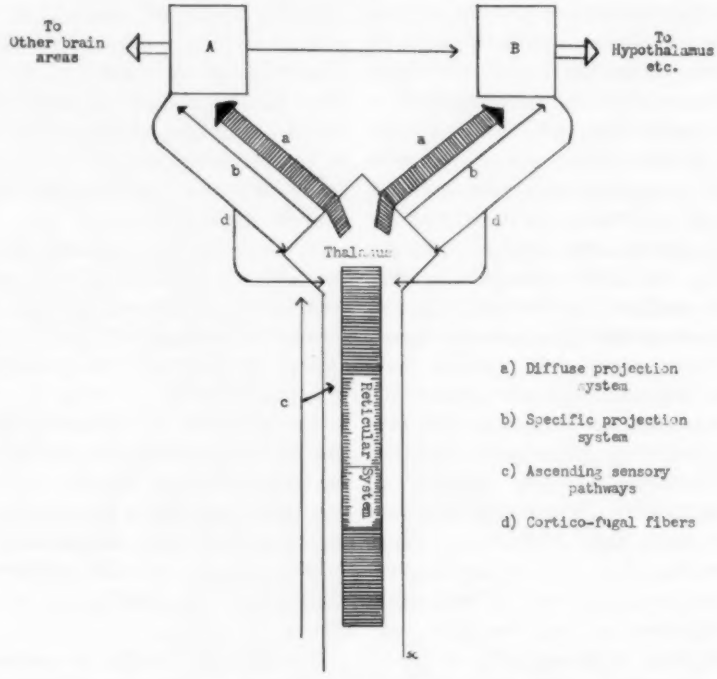
The function of "consciousness" apparently is mediated by the reticular portion of the centrencephalic system, and it may be postulated that this system, acting as a feedback regulator, may differentially inhibit or stimulate into consciousness patterns of cerebral activity—the principle of selective conation.

We may now theorize as to the manner in which such a system may operate. What follows is, of course, a gross oversimplification, with many known details omitted for purposes of illustration and clarity.

Let us suppose that a sensory stimulus enters the cortex. This sets up a spatial and temporal sequential pattern, which undergoes spread and elaboration from the sensory receiving areas, activating many neurones, which, in turn, activate others, and so on. At each step along the way, the information concerning this sequential and combinational activation is relayed by the corticofugal fibers to the centrencephalic system, where each of these activation patterns, in turn, activates an

"affective" response in the archipallium in keeping with previous conditioning (either constitutional or on the basis of past experience). The original stimulus pattern, at the same time, produces a state of unrest (reverberating activity) within the limbic system, which state is either increased or decreased by the progressive "affective" states engendered by the spreading patterns in the neocortex. The information concerning this state is transmitted through the centrencephalic system to the neocortex in the form of inhibition or facilitation of various of the simultaneous patterns being elaborated in the cortex. The inhibited patterns fade out. Eventually the facilitated patterns may enter conscious awareness, in the form of thoughts and ideas, which, in turn, may serve as new stimuli or result in conscious (volitional) activity.

Attention may now be directed more specifically toward the activity of the centrencephalic system by using the "black box" method of cybernetics, as is shown in the diagram. The sensory cortex and its association areas are represented by box *A*. The input to this box comes from the specific and diffuse projection systems. The output is by corticofugal projections to the thalamus and the centrencephalic system, as well as to box *B*. Box *B* represents those areas of archi- and mesopallium concerned with emotional experience. The input to box *B* is from the viscera (specific) and from the centrencephalic system, as well as from the sensory



The centrencephalic feedback circuit.

cortex (box *A*). The output, other than motor (autonomic), is to the centrencephalic system. If a stimulus now enters via the auditory pathways (*c*), the impulses set up discharges within the reticular system which are projected to the auditory cortex (box *A*), facilitating the specific auditory impulses and bringing the stimulus to the center of awareness. From box *A* to box *B* travel impulses setting up a state of unrest, maintained by input from the centrencephalic system. Messages from box *A* to the centrencephalic system indicate various temporal and spatial

configurations of activity within box *A*, due to elaboration of the stimulus. These messages are relayed from the centrencephalic system as input to box *B*, where they are scanned for the effects of their "affective tone" on the state of unrest. These effects are transmitted as output to the centrencephalic system and fed back to box *A* as facilitatory or inhibitory impulses, thus modifying further activity in box *A*. The elaboration of the facilitated impulses continues, transmitted as output to the centrencephalic system, with final reinforcement and perhaps consciousness within box *A* as the *recognized* stimulus. This, in turn, may act as a new stimulus, which subsequently is similarly scanned for "meaning" after the fashion already described. Subsequent activity may serve to predict the manner in which the stimulus may be effectively handled or responded to.

The centrencephalic system thereby appears to be the mechanism by which homeostasis is maintained within the brain (through the organization of cerebral functions leading to the orderly progression of thoughts and ideas, and through the integration of affect and idea to a harmonious pattern). It also contributes to the homeostasis of the organism as a whole by regulating the analytic and synthetic activity of the brain—developing patterns of behavior based on predictions of outcome as determined from past experience—which would lead to effective adaptation.

While the secondary process occupies most of our conscious attention, with resulting rational behavior and conscious judgments, the primary process continues to operate at a usually nonconscious level, influencing predictive behavior and patterns of adaptation to a marked degree. It seems fairly clear that these affective influences on rational behavior would be most marked when the affect is strong and in the nature of a defensive warning, i. e., anxiety.

It would be logical that affective behavior, which is a more direct and rapid total response than rational behavior, should be utilized automatically in times of stress.

Anxiety may arise whenever there is an extreme shift of the homeostatic equilibrium resulting from a stress which has not been offset.

In the ordinary course of events, emotionally determined behavioral patterns are developed by the organism which serve as more or less automatic behavioral or "mental" mechanisms of defense against anxiety. These mechanisms depend on effective operation of the centrencephalic and limbic systems for their success (ego strength).

In schizophrenia we postulate a disturbance to be present within the centrencephalic system. This disorder of the comparatively delicately balanced and vulnerable system results in an interference with the feedback circuits (the "traffic jam" of Wiener [29]). The functions of selective conation and emotional associations break down, giving rise to the primary symptoms. Affect is no longer coordinated with idea, and the ideas themselves are reduced to a chaotic avalanche of thoughts or impressions, which often intrude themselves upon the patient's consciousness out of context, without order, sense, or meaning. The patient is no longer master of his own thoughts or actions. Choices based on predictability of behavior are disturbed, resulting in ambivalence, self-doubt, and distrust of himself and his impulses. Unable to rely upon his own perceptions or interpretations of external events, he becomes guarded and suspicious of others. He is aware of a strangeness within himself which he cannot identify, localize, or explain, and he becomes fearful that he will be overwhelmed by some great force from within, or perhaps from without. Feeling that "something is happening" to him which he can neither understand nor control, he must find another level of adaptation or fall victim to his own anxieties and doubts. Thus, the disorganization within the secondary thought process results in regression to more primitive affective behavior, loss of ego boundaries, impaired reality testing, and a predominance of autistic thought and imagery.

This stress and the resulting marked shift in equilibrium give rise to much additional

anxiety, which the patient attempts to deal with by utilizing the defense mechanisms previously established.

In most schizophrenics the relationships formerly used as guideposts can no longer be maintained, owing to the changes which have occurred within the ego or, as we have postulated, that portion of the ego represented by the centrencephalic system. A new orientation must be found to restore equilibrium, but now it is impossible to integrate and advance. The patient finds himself "slipping" from his previous adaptation, and he struggles to maintain some sort of adjustment. The defenses to offset the anxiety are now less encumbered by reality restrictions, and projection may be utilized to an ever-increasing degree; thus, the delusional system is born.

The inability to function effectively necessitates a withdrawal from usual spheres of activity. But the withdrawal brings its own problems, and with them their own anxiety. New social, sexual, and vocational adjustments become necessary as seclusiveness, homosexual conflicts, loss of employment, etc., take their toll. Any previous manifestations of faulty or precarious adjustment now become incorporated into the symptomatology as the ego attempts to readjust itself to the new circumstances.

The success with which a new adjustment can be effected, and the efficiency with which the new (really old, more primitive) adaptive patterns function in the light of new experience, determine the level of personality integration at which the patient will operate at any given time. Failure in his adaptive mechanisms may easily lead to further regression.

A nonthreatening environment; supportive psychotherapy; educational, physical, and occupational therapy, all help to provide the support and reassurance necessary to approximate a feeling of security and to lessen anxiety, and thus help to prevent further regression. The paranoid patient with well-fixed delusions which he finds satisfactory in explaining his defects will frequently find security and escape from anxiety therein, and will be able to maintain himself on a comparatively high level of personality integration for a period of time. A failure to bind anxiety will precipitate further regression, with greater disorganization and more primitive behavior.

SUMMARY

A concept of schizophrenia as a disturbance of homeostasis is proposed.

This disturbance is believed to result from failure of a central integrating mechanism.

This mechanism is presumed normally to integrate ideational and affective processes.

Evidence is presented from the literature to lend support to these hypotheses.

A theoretical formulation is developed relating these hypothetical mechanisms to experimental and clinical data. Although our knowledge of schizophrenia is far from complete, it is hoped that this approach might serve as a useful frame of reference for future research.

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Mechanism of Syncope Due to Unilateral Compression of Carotid Bifurcation

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During the past six years we have had an opportunity to study many patients with partial or complete internal carotid occlusion in the neck.* It has been found that digital compression of the opposite carotid bifurcation results in syncope in the greatest majority of these patients (Table 1). Particularly important are the patients with partial occlusion of the internal carotid artery at the bifurcation who develop syncope on digital compression of the opposite carotid bifurcation (Table 2). The mechanical obstruction of the vessel results in an arrest or a decrease in carotid blood flow in the brain on the good side with consequent ischemia and syncope. This clinical response simulates the syncope described in the past as due to stimulation of a "hypersensitive carotid sinus" with a "cerebral type" of reaction.† Although our patients presented advanced cerebrovascular disease, it is quite likely that, even with less serious cerebrovascular atherosclerosis, patients may develop syncope by a compression of one carotid bifurcation when the opposite internal carotid is atheromatous, resulting in decreased blood flow to the circle of Willis per unit of time. Among the patients listed in Table 1 is a case of right common carotid artery ligation for an arteriovenous abnormality of the right parietal lobe. Compression of the carotid bifurcation on the left side resulted in a syncopal attack in this patient. In one patient light compression of the occluded carotid resulted in a syncopal effect associated with lowering of the pulse rate, with less blood flowing into the circle of Willis. (In this instance, apparently, the carotid sinus neural reflex vasodepressor effect upon the heart was the cause of syncope.)

In the compression test, it is important to place the fingers on the bifurcation area near the angle of the jaw, since here the vessels are more fixed and can be effectively pressed. Lower down in the neck compression may not be effective, since the vessel may slip from under the compressing fingers. Compression of the bifurcation, particularly in those patients with unrecognized internal carotid occlusion, partial or complete, on the opposite side, may be dangerous. Extreme care must be exercised to release the pressure, usually requiring 6 to 10 seconds, at the beginning of the syncopal attack. Although we have had no serious sequelae, paralysis, and even death, may result from such a maneuver.

It is apparent from the above description that when a diagnosis of the "cerebral type" of "irritable carotid sinus" has been made, the possibility of complete or incomplete internal carotid artery thrombosis on the opposite side must be considered. In cases of diffuse atheromatous degeneration of

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* References 2 to 7.

† References 1 and 8.

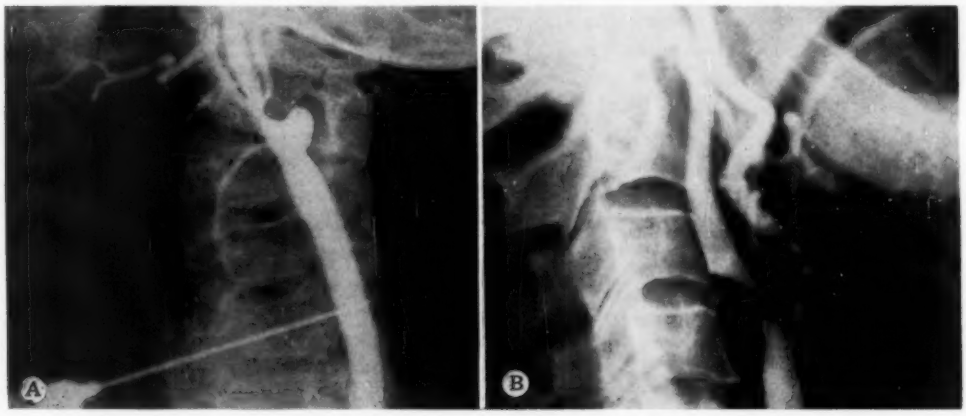
TABLE 1.—*Major Outline of Findings in Patients, with Complete Carotid Occlusion, Responding by Syncope to Compression of the Contralateral Carotid*

Case No.	Age, Yr.	Sex	Neurostatus	Angiographic Findings	Surgical Findings	Compression Result
1	54	M	Rt. chronic hemiplegia and aphasia (2 yr.); B.P. 130/86	Occlusion, internal carotid, left	Segment artery, removed	Right: Syncope, convulsive movement Left: Negative
2	52	M	Weakness, left arm and leg, gradual onset; working; B.P. 200/120	Thrombosis, internal carotid, right	Segment artery, removed	Left: Syncope Right: Negative
3	41	M	First admission: Onset with weakness, left arm, and paresthesias; transient loss vision, right eye, with episodes of vertigo Second admission (7 mo. later): Semiconsciousness, sudden onset; death 72 hr.; B.P. 165/90	I. Thrombosis, right carotid 12/2/54 II. Thrombosis, left carotid, 7/1/55 (filling of siphon from external carotid)	Segment artery, right, removed 12/10/54 Autopsy: bilateral carotid thrombosis	Left: Syncope Right: Negative
4	57	M	Rapid onset of left hemiplegia without loss of consciousness; B.P. 170/90	Thrombosis, common and internal carotid, right; thrombosis, left internal carotid	Segment artery, right, removed	Right: Hypersensitive carotid, heart block with syncope upon light palpation Left: Syncope
5	60	M	Recurrent attacks left hemiparesis; ischemia, right leg; B.P. 140/100	Thrombosis, right common carotid and right popliteal	Carotid bulb removed	Left: Syncope Right: Negative
6	61	M	Awoke in a. m. with mild paresis, right arm, confusion, aphasia; transitory blurring vision; B.P. 136/80	Thrombosis, left internal carotid	Excision, segment of artery	Left: Negative Right: Syncope, labored breathing, spasmodic movements
7	64	M	Left hemiplegia 9 yr. earlier, then acute episode of semicoma with weakness, right arm, and aphasia; B.P. 160/80	Thrombosis, right internal carotid with basilar filling; thrombosis, left internal carotid	No surgery	Left: Syncope Right: Negative
8	39	M	Sudden onset; headache and slow speech without paralysis; B.P. 140/90	Left carotid occlusion; right carotid normal; basilar normal	Excision, segment of artery	Left: Negative Right: Blurred vision, dizziness, syncope, clonic movements, bilateral
9	60	M	Mild right hemiparesis 1½ yr.; B.P. 130/80	Left internal carotid occlusion; right normal	Excision, segment of artery	Right: Bulb and common carotid; syncope and aphasia Left: Negative
10	23	M	Convulsive disorder, Jacksonian; B.P. 120/80	Massive A-V malformation, right temporoparietal area; left, normal	Right carotid ligation (uncomplicated)	Left: Syncope with bilateral clonic movements Right: Negative

TABLE 2.—*Major Outline of Findings in Patients, with Incomplete Carotid Occlusion, Responding by Syncope to Compression of the Contralateral Carotid*

Case No.	Age, Yr.	Sex	Neurostatus	Angiographic Findings	Surgical Findings	Compression Result
1	63	M	Left chronic hemiparesis with recurrent attacks during period of 1 yr.	Right: Partial occlusion, internal carotid Left: Normal	No surgery	Left: Syncope, paresthesia right arm Right; Negative
2	54	M	Collapsed with left hemiplegia and confusion; semiconscious for several hours; B.P. 130/80; gradual improvement	Partial thrombosis, right internal carotid Left: Normal Vertebral: Normal	Anastomosis, right internal and external carotid; excision bulb	Left: Syncope Right; Negative
3	39	M	"Stroke" after hemorrhaphy 2 yr. previously; weakness of left arm 11 days, then left hemiparesis, 1953; B.P. 175/120	Right: Partial occlusion, internal carotid Left: Normal	Treated by excision of internal carotid bulb with anastomosis of external carotid to internal	Left: Syncope Right: Negative
4	60	M	Vertigo and ataxia, then paresis of right arm, 7/20/55, which improved in 7 days; B.P. 130/80	Right: Narrowed common carotid and bulb Left: Narrowed internal carotid	No surgery	Right: Syncope Left: Syncope
5	59	M	History of "minor strokes" with fainting attack and vomiting 24 hr. before admission; B.P. 220/40	Right: Partial occlusion Left: Normal Vertebral: Normal	No surgery	Left: Syncope Right: Negative

cerebral blood vessels a similar effect may also be obtained when one carotid is compressed, resulting in an acute decrease of blood flow into the circle of Willis. A neural mechanism ‡ involving the sinus nerve may be responsible for an "irritable carotid sinus reflex" of the "cerebral type" in certain cases. A review of the patients reported by Ferris, Capps, and Weiss,[1] however, reveals that many of their patients may belong in the class involving mechanical ischemia of the brain due to insufficient blood flow when one carotid artery is compressed, similar to the cases above described.



Examples of angiographic findings showing complete (*A*) and incomplete (*B*) carotid occlusions in patients responding to contralateral carotid compression by syncope.

It seems reasonable to conclude that syncope unassociated with change in the pulse and blood pressure following compression of the carotid bifurcation in a patient with complete or incomplete occlusion of the opposite carotid is frequently due to an ischemia of the brain. The effects attributed to digital compression of an "irritable" carotid sinus, i. e., (*a*) slowing or arrest of the heart and (*b*) fall in blood pressure, may well be due to neural reflex responses from the bifurcation stimulation. The so-called "cerebral type" of response without such cardiovascular changes, however, in this class of patient should be reevaluated in the light of the findings reported in this paper.

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Mongolism and Convulsive Seizures

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and
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It has been recognized for many years that mongoloid mental defectives rarely have epileptic seizures. Though all who have had experience in caring for large groups of mental defectives are aware of the low incidence of convulsions in this group, there appears to have been little discussion of this finding in the literature. Kirman [1] described in some detail the case history of a patient with mongolism who developed seizures after a cerebral vascular accident with consequent extensive, but lateralized, cerebral atrophy. He also stated that in his own series of 91 cases of mongolism the patient with the vascular accident was the only one with seizures. The standard reference works either do not mention the incidence of convulsions among this group or state that it approaches that in the normal population. This rarity of seizures in mongolism is surprising if it is true that the neuropathology of this disease is essentially the same—the nonspecific type of cerebral malformations, as seen in other forms of mental deficiency. The incidence of seizures is generally regarded as high in those persons with cerebral malformations, not associated with mongolism. Earlier investigations on the electroencephalographic aspects of mongolism by Kreezer * were concerned with the possible correlation of the I. Q. and the occipital alpha activity as well as the role of the electroencephalogram in the diagnosis of types of mental deficiency. The purpose of the present study was to attempt a clarification of the actual incidence of seizures among persons with mongolism, and to determine their convulsive threshold by electroencephalographic means.

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From the University of California School of Medicine, the Sonoma State Hospital, and the State of California Department of Mental Hygiene, The Langley Porter Clinic.

Research Fellow in Psychiatry, National Institute of Mental Health (Dr. Walter).

METHOD

The clinical records of patients with a condition diagnosed as mongolism by the majority of an experienced staff were carefully searched for a history of convulsive episodes. In addition, three types of electroencephalographic procedures were undertaken.

Routine Recordings.—A total of 83 patients with mongolism had a routine, interpretable EEG examination. This consisted of an assay of the electrical activity from the major areas of the head. A minimum of 10 electrodes were applied, and a recording technique of both ear to scalp and scalp to scalp was used throughout. A sedative, usually a barbiturate, was often administered to secure cooperation and light sleep. These patients were unselected except for the diagnosis of mongolism, and ranged in age from 3 weeks to 48 years, with the mean at 15.5 years. Overbreathing for three minutes was performed in all cases in which there was sufficient cooperation.

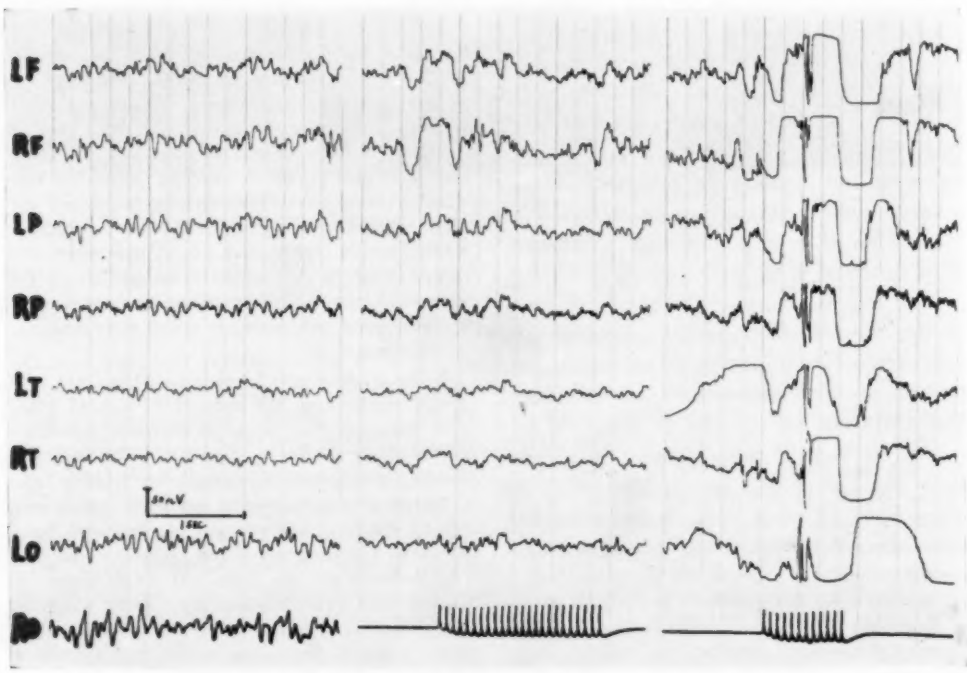
Photic Activation.—A group of 30 patients with mongolism between the ages of 13 and 45 years were examined for possible electrical activation and/or photic driving by means of a flashing light placed approximately 6 in. from the patient's face. These patients were free of any gross eye disease and did not have any evidence of congenital heart disease by routine physical and x-ray examinations. The duration of the light was a maximum of 100 μsec. and a candle-power peak beam of 120,000. The procedure was to explore all frequencies between 1 and 30 flashes per second, making both a rapid and a slow change between frequencies. It was found to be quite difficult to maintain a constant state of the eyes either open or closed because of

* References 2 and 3.

the lack of cooperation; consequently, considerable variation was encountered during the individual record. However, sections of the tracing were comparable from subject to subject, with eyes either open or closed. Any frequency of the flashing light that produced a change in the electroencephalogram was explored at some length.

Photo-Metrazol Activation.—The 30 patients tested above were also examined by a technique essentially similar to that first described by Gastaut.[4] This consisted of the rapid injection of 1 ml. of a 5% solution of pentylenetetrazol (Metrazol) intravenously every 30 seconds. Twenty seconds after the injection, the photic stimulator described above was turned on for 5 to 10 seconds at a constant flash rate of 15 per second. The 20-second delay between the injection and the beginning of the flash was an attempt to synchronize the flash with the period of maximum concentration of Metrazol in the cerebral circulation. The injection was continued until an end-point was secured in the EEG tracing. This, for the most part, consisted of high-potential, paroxysmal, multiple spikes, usually associated with a brief myoclonic jerk of the extremities. Other electrical changes consisted of mixed spikes and slow, 2-5 cps waves. Figure 1 demonstrates this, the commonest type of electrical change. At the first sign of this type of paroxysmal activity, the injection was terminated, and a barbiturate was given intravenously.

Control Group.—Patients for whom a diagnosis of undifferentiated mental deficiency had been made by the majority of the staff and who had no clinical history of seizures were used as a group for comparison with the mongolism group. For purposes of this study, "undifferentiated" indicates that there is no evidence either in the history or in the physical examination that would lead to a specific diagnosis, such as cretinism or mental deficiency secondary to infection or trauma. Included in this group of patients with undifferentiated mental deficiency were persons with high, narrow palates, various ear shapes, and other anomalies that would suggest to the clinician the strong possibility of a malformed brain. Eighty-four of the patients with such a diagnosis were examined by routine EEG tracings in the same fashion as that described for the mongolism group. Twenty-nine of these patients were matched with the mongolism patients in regard to sex and age, and these were studied both with photic activation and with the photo-Metrazol technique.



The photomyoclonic reaction. The tracing at the left was secured in a resting state. In the middle tracing 50 mg. of pentylenetetrazol (Metrazol) has been injected intravenously, and the flashing light is recorded by a photocell on Channel 8. In the tracing at the right, 300 mg. of Metrazol has been administered, and the flashing light elicits high-potential spikes, accompanied by a myoclonic twitch.

RESULTS

The records of 200 patients with a diagnosis of mongolism by the majority of the staff were reviewed. In four cases there appeared to be clear-cut, typical episodes of "spontaneous" grand mal seizures. In four other cases convulsive-like episodes were alluded to in the history, but these appeared atypical and were not documented by qualified observers. The incidence would then be 2.0% for mongolism patients with epilepsy in this hospitalized population, a figure comparing favorably with the incidence reported by Kirman.

Findings on the Routine EEG Examination.—The records on the 83 mongolism patients and the 84 patients with undifferentiated mental deficiency without epilepsy were interpreted by one electroencephalographer in the usual clinical fashion. A smaller sample of records, with any identifying data as to clinical diagnosis deleted, was interpreted by another electroencephalographer. The agreement as to general categories of the tracings approached 90%. Table 1 presents the findings in both groups when the records are classed as normal, fast, mildly or moderately slow, paroxysmal, and focal. A larger number of abnormal records is apparent in the undifferentiated group.

In addition, a measurement was made of the amplitude of each tracing on the occipital lead, recorded with the eyes closed, and averaging 50 determinations over a 10-second period. As amplitude varies with age, those patients less than 11 years of age were eliminated from both groups to make the groups more equally matched. The mongolism group had an average amplitude of 38μv, and the undifferentiated mental deficiency group had an average of 30μv. The average amplitude determined on 100 psychiatric patients, all over 11 years of age, was 28μv. The degree of organization of the record, or its degree of rhythmicity, did not significantly vary in the records from the two groups. Similarly, there were no significant changes in the frequencies of the alpha rhythms in the two groups.

TABLE 1.—*Encephalographic Findings in Mongolism and Undifferentiated Mental Deficiency*

	Normal Records	Fast	Mildly Slow	Moderately Slow	Paroxysmal	Focal
Mongolism						
Number	64	3	10	1	5	0
Per cent	77	3.7	12	1.3	6	0
Undifferentiated mental deficiency						
Number	39	11	14	5	13	2
Per cent	46	13	16.6	6.0	15.6	2.8

TABLE 2.—*Results of Photic Stimulation*

	No Response	Slight Response	Marked Response
Mongolism	7	22	1
Undifferentiated mental deficiency	8	17	4

Findings on Photic Stimulation.—In this study, the tracings secured during the period of photic stimulation were placed in three categories. In some, no clearly defined electrical response could be determined without recourse to automatic analysis. In others, the EEG changes consisted of evidence of "following," in which the cortical rhythm assumes the same frequency as that of the flashing light. Some records exhibited a marked response at various frequencies, either in the amplitude of the response or in its appearance over the entire surface of the head. The findings in the two groups are recorded in Table 2. No prominent difference between the two groups is apparent. However, one of the patients with undifferentiated mental deficiency without epilepsy responded consistently with paroxysmal spiking at frequencies of 10 to 20 cps. This finding can be interpreted as showing a very low threshold insofar as susceptibility to convulsive phenomena in response to a flashing light is concerned.

Photo-Metrazol Determinations.—A clear-cut difference in the photomyoclonic threshold between the two groups could be demonstrated. An average value of 6.9 mg kg. of Metrazol was obtained for the mongolism group and an average value of 4.7 mg/kg. for the group of patients with undifferentiated deficiency without epilepsy. Table 3 demonstrates the distribution of the

patients in the two groups in regard to their individual threshold values. The critical ratio of the difference between the means of these distributions is 4.25, which is significant at a level of $p<0.001$.

In spite of a good deal of caution, generalized seizures were induced in 5 of the 59 patients, giving an incidence of 8.5%. It is recognized that expressing the threshold in milligrams per kilogram may not be the most accurate way. However, no relationship could be established between the photo-Metrazol threshold and the age or sex of the patients. Larger doses of Metrazol were necessary to produce the desired end-point in those subjects with greater weight.

TABLE 3.—*Individual Results on the Photo-Metrazol Determination Expressed in Terms of Milligrams of Metrazol per Kilogram of Body Weight*

Mongolism (N-30)	Undifferentiated Deficiency Without Seizures* (N-28)	Mongolism (N-30)	Undifferentiated Deficiency Without Seizures* (N-28)
3.6	2.4	7.3	4.5
4.3	3.0	7.5	5.0
4.4	3.1	7.7	5.2
4.7	3.1	7.7	5.4
4.8	3.2	7.8	5.5
4.9	3.3	8.0	5.7
5.3	3.7	8.1	5.8
5.4	3.8	8.2	6.1
5.7	3.8	8.3	6.9
5.7	4.0	8.3	7.5
6.1	4.0	8.3	7.9
6.5	4.0	8.5	8.5
6.6	4.1	8.7	9.6
6.8	4.1	9.5	...
7.1	4.2	13.0	...

* Exclusive of the one case among those of undifferentiated mental deficiency that showed a paroxysmal reaction to light alone; the critical ratio of the difference between the means is 4.25, with $p<0.001$.

COMMENT

It would appear from the preceding data that patients with mongolism as a group tend to have EEG tracings approaching those found in the normal population. The average amplitude, however, is considerably higher than that for the control group or for psychiatric patients in general. The photo-Metrazol threshold is also in a range approaching that for the "normal" population. This is in contrast to the control group of patients with undifferentiated mental deficiency without epilepsy, who have a considerably higher incidence of EEG abnormality and a markedly lower photo-Metrazol end-point. The possibility exists that the difference in the photo-Metrazol thresholds could be explained by the high incidence of opacities of the lens in mongolism, as recently discussed by Igersheimer and Mautner.[5] However, this explanation seems unlikely in view of the nearly equal electrical reactions to photic stimulation in the mongolism group and in the undifferentiated (control) group. From this evidence we have considered the light stimulus to be above the threshold for these patients.

Malamud[6] has recently presented a statistical analysis of the neuropathological findings in 543 autopsied cases from the Sonoma and Pacific State Hospitals. He found that in the pathological group with cerebral malformations there was a high incidence of positive neurological signs and convulsions, with the exception of the mongolism cases. Judging from his report, the neuropathological findings in mongolism, and presumably in our control group, would consist of nonspecific types of malformations, such as anomalous temporal lobes, convolutional irregularities, and cytoarchitectural alterations. In a recent small survey of the electrical activity associated with malformations observed at autopsy in the group with undifferentiated deficiency, we have been impressed by the high positive correlation with EEG abnormality.† If the neuropathological changes in the two groups of patients studied could be expected to be similar, why is there such a discrepancy in the amount of "abnormal" electrical activity and such a marked difference in the photo-Metrazol thresholds?

Kirman states that the reason for the lower incidence is the absence of focal neuropathology in the patients with mongolism. This explanation seems inadequate, however, when one considers the high incidence of seizures in patients without mon-

† Unpublished data.

golism but with generalized, rather than "focal," cerebral malformations. The possibility also exists that these electrical findings can be explained by a quantitative difference in the amount of neuropathology between the group with mongolism and the group with undifferentiated mental deficiency. Malamud [6] states that such malformations as the anomalous temporal lobe can be equally demonstrated in cases of mongolism, agyria, microcephaly, and oligoencephaly. This would imply a lack of any pronounced quantitative difference in the degree of pathology between the two groups in this study.

Benda [7] does not discuss the possibility of any relationship between mongolism and the absence of seizures. He reviews in detail the question of metabolic and/or endocrine disorders in this disease and concludes that nearly all of the single measurements fall within the normal range, but this does not exclude the possibility of metabolic disease. A consistent alteration in glucose metabolism was described, with a low fasting blood sugar, an increased sugar tolerance, and a lack of response in the blood sugar curve to epinephrine. Recently Simon and associates [8] have reported a change in the amount of large molecule lipoprotein of the S_f 12-20 class. Though, by and large, the metabolic and endocrine alterations have not appeared dramatic as measured by present tests, it is tempting to explain the higher threshold and more "normal"-appearing records on the basis of some unknown metabolic or endocrine derangement producing a hypoexcitability of the nervous system.

SUMMARY

In this study, the incidence of convulsive activity in mongolism was found to be 2.0%. The electroencephalographic picture and the reaction to photic stimulation approach those of the "normal" population, in contrast to a control group with undifferentiated mental deficiency without epilepsy. However, the mongolism group demonstrated a higher potential of electrical activity recorded from the scalp than did the group with undifferentiated deficiency, or unselected psychiatric subjects. With the photo-Metrazol technique, the photomyoclonic threshold was found to be high for the mongolism group and close to the thresholds for "normal" controls reported in other studies, and low in our group with undifferentiated mental deficiency. The factors producing these signs of electrical normality in the presence of the neuropathological changes of mongolism are unknown and need further investigation.

Edward Jewett, M.D., Clinical Director at the Sonoma State Hospital, cooperated in this study, and Ruth Lawrence secured many of the records.

University of California Medical Center at Los Angeles (Dr. Walter).

The Langley Porter Clinic (Drs. Yeager and Rubin).

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Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Erich Lindemann, M.D., President, Presiding
Regular Meeting, March 17, 1955

Pathology of Parkinsonism. Dr. J. G. Greenfield.

On the occasion of the 200th anniversary of the birth of James Parkinson the speaker discussed the present status of the pathology of paralysis agitans. Lesions in the substantia nigra have been recognized since 1919 as the basis of postencephalitic Parkinsonism, but the pathology of idiopathic paralysis agitans has been considered in English-speaking countries rather to be in the corpus striatum and globus pallidus. This view derives especially from the Vogts' (1920) monograph, but their cases were not all typical and their examination of the substantia nigra was admittedly incomplete. Their pupil Hassler (1937-1939) mapped the normal substantia nigra and found constant loss of certain cell groups in typical paralysis agitans. He also emphasized the presence of hyaline inclusion bodies, first described by Lewy (1913), in the cells of the substantia nigra and locus caeruleus in this disease.

Klaue (1940), Beheim-Schwarzbach (1952), and Greenfield and Bosanquet (1953) have confirmed the constancy of these lesions in the substantia nigra. The last authors differ from Klaue in considering Lewy inclusions characteristic of the idiopathic disease. In postencephalitic cases they found fibrillary changes of the Alzheimer type in the pigmented cells of the brain stem with equal constancy.

DISCUSSION

Dr. D. Denny-Brown: Parkinsonism is, I suppose, one of the most difficult problems in neurology from every conceivable aspect, not only from the clinicophysiological but also from the anatomical and neuropathological. There have been many attempts to define one structure damage to which results in Parkinsonism. Most experimental work has suffered from the oversimplification of our clinical descriptions. The more intense the Parkinsonian tremor becomes, the more it involves motion, just as cerebellar tremor in the more intense form disturbs posture. Electromyographic studies give no clear-cut manner of defining Parkinsonism from other types of tremor. Study of tremor produced by damaging midbrain and subthalamic structures convinces one that whatever causes Parkinsonism must be a very diffuse kind of pathology. The classical studies of the neuropathology of Parkinson's disease clearly indicates the diffuse nature of the changes. Which are the primary changes and which are secondary (transneuronal)? I have long hoped that a neurocytologist of the caliber of Dr. Greenfield would take up this subject. It is clear that he has at once brought into focus the intimate changes in nerve cells and has shown how consistently two types of change reflect the two main types of Parkinsonism. The clinical significance of the prominence of such changes in the substantia nigra and in the locus caeruleus is still not answered. One is immediately reminded of other diffuse diseases of the nervous system, such as Wilson's disease, where focal damage does not necessarily account for the dominant symptomatology. Though one has no doubt that these neuronal changes must be primary in this disorder, there still remain problems, such as the meaning of the special liability of pigmented cells and the real nature of these inclusions. Is it possible that the same process affecting the globus pallidus does not produce inclusions only because the cells in that location are not pigmented?

The Lafora bodies in myoclonic epilepsy are also found in the substantia nigra. There is a link between myoclonic epilepsy and Parkinson's disease. In Hassler's paper, the case of Parkinsonism that showed the best inclusion bodies was also a familial one. Therefore, if we try to relate these inclusions in terms of what we know, it is in these familial diffuse neuronal diseases, whose most obvious form is the lipidoses. We still have a long way to go before we can put Parkinson's disease clearly into that category, but Dr. Greenfield's observations point in the direction of this etiology.

DR. STANLEY COBB: I have always been a little confused about the nomenclature, and I think I understand that Dr. Greenfield uses it in the way I do. I would say that Parkinson described the shaking palsy, or paralysis agitans, and that therefore people who divide the disease into "paralysis agitans" and "Parkinson's disease" are making a false distinction. If I understand rightly, Dr. Greenfield, you divide Parkinson's disease into two kinds: "idiopathic," the form originally described, and the more recent one, which appeared with the epidemics of encephalitis, i. e., "postencephalitic." If we could agree on this terminology, it would be helpful.

In some brains I looked over with Dr. Benda, we thought there were significant vascular changes in the striatum and in the cortex, especially in Area 6, and I think we stressed the cell loss. You laid your emphasis, rightly from the modern point of view, on these inclusion bodies. Do you believe that the vascular changes are significant? Are the areas of cell loss so general that we need pay no attention to them?

It is hard not to mix in our physiological ideas and fantasies and our surgical ideas with the pathological. I think the neurosurgeons have, by their experiments on the human, made some interesting observations which we must use in understanding the physiology. Parkinsonism is a disease in which animal experimentation will never be satisfactory because the motor apparatus, even of the higher monkeys, is not the same as in man.

DR. PAUL I. YAKOVLEV, Middleton, Conn.: Would Dr. Greenfield, from his experience, amplify on the interesting possibility alluded to some 30 years ago by Foix and Nicolesco, that in Parkinson's disease the pathological alterations affect with a certain selectivity the pigmented system of nuclei of the tegmentum: the substantia nigra, the locus caeruleus, and the chain of pigmented cells scattered in the brain stem? Might Dr. Greenfield be willing to suggest the possible significance of this curious system of cells? As Dr. Denny-Brown has just indicated, there are indications that Parkinson's disease may be envisaged as a metabolic disorder of the nervous system. The intracellular inclusions which Dr. Greenfield described would seem to point in the same direction. On general grounds one is inclined to consider that the system of pigmented cells in the brain stem may be related in some way to visceral functions and may represent some autonomic or vegetative mechanism in this sphere of physiological activity.

DR. CLEMENS E. BENDA: In 1942 Stanley Cobb and I published one of the few pathological studies on paralysis agitans, celebrating at that time the 125th anniversary of James Parkinson's immortal essay on the shaking palsy (1817). The actual neuropathological work was done in 1936, a year before Rolf Hassler (of the Institute of the Vogts) published his study in which the original concept of the Vogts—that paralysis agitans was a disease of the striatum—was revised and the importance of the substantia nigra in all cases of paralysis agitans emphasized.

It is worth while to remember that at the time of our studies it was the undisputed dogma of American neurology that alterations in the substantia nigra were found in postencephalitic Parkinsonism but that paralysis agitans had a different neuropathology and was a disease of the putamen, globus pallidus, and other areas. Our paper established for the first time that cases of paralysis agitans showed severe alterations in the substantia nigra, which are well established for the postencephalitic condition. It is a great satisfaction to me to see that after 20 years Dr. Greenfield fully confirms our findings.

As to the so-called "inclusion bodies," we were not certain at that time about the pathological significance, and many contemporaries felt they might be artifacts; so we did not dare to put any emphasis on this point. It would be a great satisfaction to the late F. H. Lewy, who can be at least partially claimed as a past member of the Boston community through his long association with the Cushing Hospital, to see that the inclusion bodies which he described as early as 1914 have finally found general recognition and are established in their pathological significance, although the nature of the metabolic disorder underlying their formation is still not known.

As Dr. Cobb mentioned in the discussion, we found some evidence in our material of vasoparalytic stagnation of blood flow, with unusual enlargement of vessels and perivascular spaces, an observation which had also been emphasized by the Vogts in their term of status cribrosus and reemphasized by Hassler. I would like to know whether similar observations have been made in Dr. Greenfield's material. These data would be of interest to the clinician, because some of the successes of therapy may depend upon achieving a better circulation through the brain.

DR. J. G. GREENFIELD: Not being a clinician, I cannot answer Dr. Denny-Brown's question about the nature of the tremor. With reference to his comment about the inclusion bodies, Lafora

pointed out the marked histological distinction between the bodies seen in myoclonus epilepsy and those seen in paralysis agitans. With some staining methods they cannot be confused. There may be some metabolic connection between them, and both may be a familial condition. We are still finding cases of familial progressive myoclonus epilepsy with typical Lafora bodies, and we do not find them in paralysis agitans. I am entirely in agreement with him that we are concerned with some metabolic change. I hope that before long we shall know more about the metabolism of the nerve cell, and so find a way to stop the progress of the disease.

Dr. Cobb emphasized the distinction between Parkinson's disease and Parkinsonism. In general, there are many cases in which it is difficult to say whether they are postencephalitic. With a more rapid onset, and in younger people, the disease is more likely to be postencephalitic. In one or two of our cases which came on rapidly, with severe destruction of the substantia nigra, we could not make a distinction. He has also raised the question of the significance of vascular changes in the striatum and cortex. Much of our material was old, and it was therefore impossible to use all the staining methods we should have liked; but it was our impression, in going over a large number of basal ganglia, that vascular changes were not greater than those common at the same age. I think Hassler's last paper is important from that point of view. I find it difficult to understand how a perivascular loss of cells can produce such a peculiar range of symptoms. The greater loss of small cells than of large ones, which the Vogts found in paralysis agitans, is described also in chorea. It is difficult to see why one kind of symptom should occur in one disease, and another kind in another disease, after the loss of the same cells. The work of Benda and Cobb was important, but we were unable to follow it up in any large series because our sections did not include Area 6. To make any assessment of the importance of changes in this area would mean a large survey of other areas, and this we were not able to do in the time we had.

I am quite unable to answer Dr. Yakovlev's question. I do not know anything about the function of these pigmented cells. One does not consider the pigmented cells to be the only structures involved, or the only ones in which Lewy inclusions may occur. They have been found by many workers, starting with Lewy, in the substantia innominata also. This is another area about the physiology of which we know little and which deserves further study.

I cannot answer Dr. Benda's question about early cases because we had no material of that type.

CHICAGO NEUROLOGICAL SOCIETY

Benjamin Boshes, M.D., *President*

Oscar Sugar, M.D., *Secretary*

Regular Meeting, April 12, 1955

SYMPOSIUM ON THE TEMPORAL LOBE

The Temporal Lobes and Auditory Pattern Discrimination. DR. I. B. DIAMOND (by invitation).

We have performed a series of ablation experiments using cats and monkeys in which the ability to discriminate between tonal patterns or rhythms was compared before and after making lesions of various sizes in the "temporal" region of the cortex. In some cases the operations were guided by evoked potential maps; for most animals the area around the lesion was exposed before the animal was killed to determine whether cortex responsive to tonal pulses remained; in all cases the brain has been or is being studied histologically.

In cats the amount of degeneration in the medial geniculate body is proportional to the size of the cortical lesion. With lesions confined to AI (Rose and Woolsey, 1949), only the posterior half of the medial geniculate body degenerated. Even with lesions more extensive than AI, AII, and Ep, the posterior tip of the medial geniculate body appeared normal. In sharp contrast to this finding is the relationship between the behavioral effect and the size of lesion. Where a small fragment of cortex was found to be responsive to tonal pulses, the cat was able to discriminate between tonal patterns or rhythms. When all responsive cortex was removed, the animals were unable to make these complex discriminations. Histological study of the monkey brains is not yet complete; but, from our surgical notes, we expect comparable results from monkeys.

We would not conclude from this investigation that evoked potential maps are the only adequate statements of functional units. We would argue that behavioral effects can be considered, along with conventional anatomical procedures, as a criterion for analysis of the cortex into parts.

Multisensory Timing Ability in Persons with Lesions of the Temporal Lobe. DAVID SYMMES (by invitation).

This report is concerned with the description of a new behavioral test which is designed to discriminate between the absence of functional tissue in the temporal lobe and the normal condition of that structure. Some theoretical justification for an approach through the basic ability to perceive time intervals is attempted. The test described purports to measure the accuracy with which temporal intervals are perceived when based on information received via three different modalities: audition, vision, and touch. Scores on this test by four classes of subjects are reported: (1) a group of epileptic patients having focal spiking in the temporal lobe, (2) a group of patients having had unilateral excision of the anterior temporal lobe for the relief of focal epilepsy, (3) a group of nontemporal neurosurgical patients, and (4) a group of normal controls. The data suggest that the auditory problem is nondiscriminating, while the visual and tactual problems reveal varying degrees of impairment. The impairment is maximal in those cases with focal spiking in the temporal lobe, diminishing toward normality in the surgical group. Some of the most successful surgical cases were not differentiated from normals by the present test. The theoretical significance of the results was explored, with brief attention to the scores of the nontemporal surgical cases.

Some Frontotemporal Lobe Relationships. DR. WARD C. HALSTEAD.

The Halstead battery of neuropsychological tests has proved sensitive in several recent studies in detecting unilateral frontal lobe lesions in man against appropriate controls ($P<0.001$). This battery is not sensitive for unilateral temporal lesions in spite of the anatomical intimacy of frontotemporal connections.

Several new indicators have been developed which appear to bear upon temporal lobe functions. These include a Multi-Sensory Timing Test (Mr. David Symmes); the Auditory Flutter Fusion Test, which appears to be an analogue of critical fusion frequency, and an Auditory Pattern Association Test. This new battery detects unilateral temporal cases at the 0.01 level of confidence.

Surgical Aspects of Temporal Lobectomy in Man. DR. L. V. AMADOR (by invitation).

From the large number of psychomotor epileptics, we have chosen a group which had a long history of seizures that had not responded to intensive anticonvulsant medications. Patients who were suspected of having brain tumors were not included in the group of cases to be presented. A total of 90 operations were carried out on 72 patients. Twelve of these operations were stereotaxic implantations of electrodes into the temporal lobe in order to delineate the discharging areas more accurately. These cases later had a temporal lobectomy. From a study of the carefully placed depth electrodes it can be seen that the focus, which was once thought to be in the tip by some investigators, appears to be a shifting area of abnormal electrical activity in the entire temporal lobe, and in some cases in the Island of Reil.

The usual resection consisted of removing the anterior and lateral portions of the temporal lobe, a distance of approximately 6 cm. from the tip. The medial extent was usually to the amygdala. In some of the cases where the abnormal discharges were more extensive, it was necessary to resect larger portions of the temporal lobe, and in some cases the lateral surface of the Island. All cases had thorough electroencephalographic investigation by Dr. Gibbs before, during, and after surgery. Pathological alterations included chronic gliosis, in 10%; thickened arachnoid, in 10%; meningocortical scars, in 6%, and chronic neuronal changes, in 10%. Several tumors were unexpectedly discovered and removed. Postoperatively there were a few cases of temporary, partial aphasia (7%) and some confusional episodes. Mortality was zero.

Psychological Findings After Temporal Lobectomy in Man. Dr. Marianne L. Simmel (by invitation).

All those patients who have been operated by Dr. Amador since the fall of 1952 have been examined by us extensively prior to surgery, three months after surgery, and 15 months after surgery. After exclusion of 5 patients who were found to be either psychotic or feebleminded before operation, or had undergone previous brain surgery, there remains a group of 17 patients, 13 male and 4 female, ranging in age from 18 to 45 years at the time of operation. Fourteen of the patients are right-handed, and in two-thirds surgery was performed on the dominant hemisphere. Of the 17 patients, 8 report no seizures currently; 5 report some improvement, and 4 report no change. In addition to psychomotor attacks, eight of the patients had grand mal seizures before surgery; at the present time none of the patients has grand mal attacks. Those patients who were employed despite seizures until shortly before surgery are once more working, some of them with seizures, while those who had been unemployed for an extended time before surgery are not working now, despite absence of seizures in the case of some of them. One seizure-free patient is in a state hospital, where he had been on several occasions before operation. On the basis of informal clinical impression, it would appear that 4 of the 17 patients have shown increasing personality disorganization, while 3 have made marked progress in overcoming their difficulties. The remainder show no gross changes from their preoperative psychiatric status: Some of them were pretty well organized before surgery and are so now; others we thought were precariously balanced then, and they still seem so. Those experimental data which have been analyzed to date indicate no change from before to three months after surgery in a variety of tests, including standard intelligence tests and experiments concerning the estimation of time.

DISCUSSION ON PAPERS ON THE TEMPORAL LOBE

Dr. Percival Bailey: As you know, I have been interested in the brain for a long time, and I have never believed that any part of the brain does not have any function, or that you can take it out without producing a defect of some kind. If you do not find the defect, it is because you do not know what questions to ask. I have always encouraged Dr. Halstead to try to find out what questions to ask. He began with the frontal lobe cases because those were most frequent, and you all know how successfully he has worked with this problem. When Dr. Gibbs got me interested in cases of temporal dysfunction, in psychomotor epilepsy, we again tried to find similar questions.

You must realize that the lobes of the brain are very crude anatomic subdivisions. These lobes were named originally after the cranial bones under which they lie. They are not functional subdivisions of the brain in any sense of the word; so when we talk about frontal or temporal lobe functions, we are using very unscientific and nonspecific terms. The temporal lobe has obvious functional subdivisions. In the first place, it contains the primary auditory projection, and about it certain very definite facts are known. There are what we call the periacoustic and the acoustic areas, and the two together form a functional unit. Then, besides that, we think of another area, the anterior portion of the temporal lobe, which has very few connections with the areas I have just spoken about. If we put strychnine on the tip of the temporal lobe, it does not affect the auditory or periacoustic area and vice versa; so obviously there is a functional difference between these two. Then, in addition, there is a third area, which lies on the lower surface of the temporal lobe in animals, and on the undersurface of the third temporal convolution in man, that is, again, quite different; this area myelinates very late and was included by Flechsig in his associational areas. In addition, the posterior part of the temporal lobe has connections with the acoustic area and the striate and parastriate visual cortex.

When we talk about a psychomotor case, we are talking about this anterior portion of the temporal lobe, anterior to the lower end of the central sulcus. It has no very close connections with the acoustic area; so if you tested these cases for auditory function, whether primary audition or time lapse, I would not expect them to show any very great difference from normal. On the other hand, if you carried the extirpation in to the periacoustic or acoustic area, you might expect a very definite defect in this function. Personally, I am not surprised that you have to use a statistical method in order to find evidence of defect in these functions. Anatomically, I would expect to find a defect of some sort in psychological function connected with the viscera, because the medial portion of the temporal lobe, which is connected very closely with the anterior portion, is concerned with visceral function. If it is stimulated electrically, a most intense disturbance of

respiration results, and the visceral nerves project to this portion of the temporal lobe. There should, therefore, be some defects in higher functions connected with primary visceral functions, such as taste and smell. The psychologists have not been able to devise tests in this field but prefer to continue testing with procedures with which they are familiar and which have been found useful in previous studies of other regions of the brain. The reason we do not get very great differences between frontal and temporal lesions, when tested with these traditional tests, is that there is a powerful uncinate tract binding these areas together. We may expect, therefore, only shades of difference, because they have various connections with other areas, besides powerful connections with each other.

So much for the psychological differences to be expected after lesions of the temporal lobe. Just a word about what happens if the lobe is removed on both sides. We have been very careful not to enter into the medial portion of the temporal lobe on both sides because of the experience of Drs. Klüver and Bucy. We have stayed carefully lateral to the lateral horn of the ventricle, except in one or two severe cases, where we invaded the medial surface on one side. Others, however, have not been so careful. Just recently there came to my desk a description of a combined Klüver-Bucy syndrome produced by complete bilateral temporal ablation. There was the whole picture, with nothing missing. I should like to point out, therefore, that we have been doing these extirpations in a somewhat experimental manner in man, but we have been doing them with all the precautions set down by the A. M. A. Committee on Ethics to guide such physiological experimentation on man. That is to say, we have used every precaution to be sure that we do no harm to the patient, and we have always obtained the consent of the patient if he is capable of giving that consent, or the consent of the responsible guardian in case he is not. In operating, you have heard how little disturbance we have caused these patients; none has died; if the operation is done for mental disturbance, the patients have as a rule been so little disturbed that the psychologists have to resort to statistical analysis to find that we have caused a defect in any way. In a few cases we have altered the general behavior for the better and have suppressed the epileptic syndrome in a great number. What will be the ultimate result? We cannot say, because our experience with epilepsy has taught us this, that at least five years must pass after operation before you can begin to estimate the probable result. We started doing this operation in 1947, and most of the cases have been done in the last two or three years. We expect to continue to do extirpations, following always the rules which I have mentioned, and taking all possible precautions that we do not cause the patients any harm.

DR. R. M. REITAN, Indianapolis: We have been testing patients from the neurological and neurosurgical services of the Indiana University Medical Center for nearly the last four years, spending a day and a half to two days in individual testing of each patient. Our patients can probably be classified into three groups: those with indications of rather widespread brain damage; patients with intrinsic tumors, the limits of which are very difficult to define, and a much smaller group, with lesions fairly well restricted to a particular area.

It seems to me that the questions that have been posed this evening are ones concerned with the function, or at least a loss in function, associated with lesions in a particular area. In other words, the question has been raised of localization of function of a particular part of the brain. This is a very difficult question to approach with human clinical material, particularly in consideration of the frequent occurrence in many patients of rather widespread vascular involvement, intracranial hypertension, cerebral edema, the effects of early trauma, and the many things that may be present. Since possible effects of localizing significance may well be obscured, rather than clarified, by failure to evaluate these many distracting factors, we have accumulated so far only a small group with localized temporal lesions. The small size of our samples limits the possible generality of our findings.

I think we can draw very tentative conclusions, which may be of some interest in relation to the type of findings that have been presented this evening. One thing that stands out is that patients with lesions in the right temporal lobe, which probably involve only that lobe, have a very definite difficulty on a particular test. This test (Picture Arrangement Subtest of the Wechsler-Bellevue Scale) requires that the patient arrange pictures in a temporal sequence. The test consists of a number of problems. The first problem is very simple, consisting of a picture of a bird building a nest, a picture of the nest completed in the tree, and a third picture, of baby birds being fed by an adult bird. The patient is asked to put the pictures in the right order. The problems become more difficult as the test progresses. Patients with lesions restricted

to the right temporal lobe seem to have a very definite difficulty with this test. They have trouble effecting the temporal relationships indicated. I don't know how closely this may be related to difficulties in temporal pattern discrimination and other auditory tests which have been discussed, but it seems to me that there may be a relation in that both require sequential temporal ordering. This may be the important factor, rather than auditory function as such. Interestingly enough, in patients with lesions in the left temporal area, we fail to obtain evidence of this defect. These patients generally perform better on this test than they do on the other tests given.

On the basis of these findings, it seems to me that there may well be a distinct difference in the function of the right, as contrasted with the left, temporal area in right-handed human adults.

DR. I. DIAMOND (by invitation): In connection with Dr. Bailey's remarks, I would like to comment that we have been very much concerned with the definition of the auditory areas of the cortex. An adequate comparison of our behavioral results in cats and monkeys depends on our ability to delimit homologous regions. The question of boundaries is complicated by the fact that the method of evoked potentials and the method of retrograde degeneration do not yield identical maps. Many problems thus remain from the purely anatomical point of view. The point that has struck us is that after an ablation of the cortical areas both cats and monkeys suffer an irreversible loss of pattern discrimination in response to click stimuli. A smaller lesion, confined to the "essential" projection of the medial geniculate body, has no effect. It is tempting to consider the minimal region necessary for a particular kind of behavior as an additional criterion for defining a unit of the nervous system.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

PERIPHERAL NEURITIS AS A SEQUELA OF CARBON MONOXIDE ASPHYXIATION. H. RENFERT JR. and A. DREW, Ann. Int. Med. **42**:942, 1955.

Renfert and Drew report a case of carbon monoxide asphyxiation in a 50-year-old white man that was followed by a peripheral neuritis in the distribution of the left ulnar and sciatic nerves. This complication occurs infrequently and is manifested by burning sensations, shooting pains, and hypalgesia along the involved nerve trunks. These symptoms occur, in addition to mental changes. The neuritic symptoms persist longer than the original acute symptoms and may clear with vitamin B therapy.

MANDEL, Philadelphia.

SOME EFFERENT CONNECTIONS OF THE HUMAN FRONTAL LOBE. A. MARTINEZ, J. Neurosurg. **12**:18, 1955.

Two cases of frontal leucotomy were studied by means of the silver impregnation technique of Gros in order to determine the course and termination of the corticofugal fibers in the subcortical nucleus. Lesions upon the medial surface of the frontal lobe were reported by the author to show degenerated nerve fibers and hypertrophied *boutons terminaux* in the medial mammillary nucleus. When the lesion was present in the prefrontal area, degenerated fibers were present in the dorsal medial nucleus of the thalamus, the subthalamic body, and the lateral nucleus of the hypothalamus. Corticopontine fiber degeneration was also present in one of the two cases studied.

MANDEL, Philadelphia.

Physiology and Biochemistry

SYDENHAM'S CHOREA: I. EVIDENCE OF ABNORMAL ADRENAL CORTEX FUNCTION. L. E. AINGER, R. S. ELY, A. K. DONE, A. B. BRILL, and V. C. KELLEY, A. M. A. Am. J. Dis. Child. **89**:575, 1955.

The authors studied 30 patients with Sydenham's chorea. Slight but significant elevation in the mean concentrations of serum mucoproteins and hexosamines (in both, $P<0.01$) was observed, although the majority of the individual values obtained still fell within the normal range. The nonglucosamine polysaccharides were found to be quite consistently elevated beyond the normal range. The mean value for this group not only was significantly ($P<0.01$) greater than the mean of the normal group but exceeded the upper limit of the normal range. These alterations in the acute phase reactants in Sydenham's chorea may reflect alterations in function of the adrenal cortex.

In addition, alteration in function of the adrenal cortex is supported by observations concerning circulating concentrations of pituitary and adrenal hormones. Almost all the patients studied in this series had abnormally low levels of circulating 17-hydroxycorticosteroids. Several of them had simultaneously elevated levels of endogenous corticotropin. These findings are interpreted as indicating a state of relative adrenocortical insufficiency in patients with Sydenham's chorea. That it is relative and not absolute is demonstrated by the adequate increase in plasma 17-hydroxycorticosteroids in response to the administration of corticotropin, although the amount of corticotropin administered was considerably greater than the total amount of circulating endogenous corticotropin found in the patients. This altered state of adrenocortical function was present in these patients whether or not there were exudative manifestations of the disease and whether or not there was elevation of the erythrocyte sedimentation rate. The latter observation suggests that classification of chorea as of psychogenic origin because of a normal erythrocyte sedimentation rate is open to question.

Regardless of the mechanism producing this relative adrenocortical insufficiency, the equilibrium state with regard to the levels of 17-hydroxycorticosteroids indicates that the adrenal cortex is not producing these steroids rapidly enough to maintain a normal concentration in the blood.

SIEKERT, Rochester, Minn.

CONTRIBUTION TO STUDY OF WILSON'S DISEASE. V. GILSANZ, J. M. SEGOVIA, and H. C. MENDOZA, A. M. A. Arch. Int. Med. **95**:727, 1955.

The authors report the results of metabolic studies in a family in which two members have clinical and metabolic symptoms of Wilson's disease and a third has amino-aciduria as the sole symptom. All three cases had an amino-aciduria which preceded by several years the clinical onset of the disease. There is an increased amount of ammonia formed in the kidney in Wilson's disease, which is dependent upon the degree of amino-aciduria. However, the amino-aciduria is not the direct cause of elimination of copper by the kidney, nor is it responsible for retention of copper in the body. Corticotropin caused an increase in the excretion of amino acids but had no effect upon the elimination of copper. Dimercaprol (BAL) increased the elimination of copper without affecting the amino acids. This lack of parallelism between the administration of corticotropin and that of dimercaprol demonstrates that copper is not bound to amino acids eliminated in the urine, as has been previously considered.

The authors believe that Wilson's disease should be considered as a congenital familial alteration with a lack of enzymes necessary to break down peptides into amino acids. The protein metabolism would, therefore, be arrested in the stage of dicarboxylic oligopeptides, which deposit in the liver, basal ganglia, and cornea of the eye. These peptides have a great affinity for copper, with the resultant deposition of copper in these tissues. The copper which is passed in the urine is bound to the oligopeptides, and not to the amino acids.

MANDEL, Philadelphia.

THE INFLUENCE OF SHOCK ON CEREBRAL HEMODYNAMICS AND METABOLISM. J. P. FAZEKAS, J. KLEH, and A. E. PARRISH, Am. J. M. Sc. **229**:41, 1955.

The cerebral hemodynamics and metabolism of 11 patients in shock were studied by the technique of Kety and Schmidt. The mean arterial pressure varied from 20 to 76 mm. Hg. The cerebral blood flow was 31.5 cc/100 gm. of brain/min., which is less than that of normal subjects. There was no correlation between the rate of blood flow and the state of consciousness. The cerebral metabolic rate was also reduced to a mean value of 1.9 cc/100 gm. brain/min., with a range of 0.5 to 3.6 cc/100 gm. brain/min. The ability of the cerebral cells to extract large amounts of oxygen from the blood is indicated by the low venous oxygen levels. The good state of cerebral function in the presence of reduced blood flow may be attributable to a capacity of the cerebral cells to compensate by extracting larger amounts of oxygen.

BERLIN, New York.

THE STRUCTURE OF CEREBROSIDE SULFURIC ESTER OF BEEF BRAIN. S. J. THANNHAUSER, J. FELLIG, and G. SCHMIDT, J. Biol. Chem. **215**:211, 1955.

Cerebroside sulfuric ester was first isolated from beef brain in 1933. Recently, a method has been described for separation of the pure substance. The present communication shows that the sulfuric acid group is on the primary hydroxyl of carbon 6 of the galactose portion of the molecule.

PAGE, Cleveland.

STUDIES ON THE CONJUGATED LIPIDES: VI. ON THE STRUCTURE OF INOSITOL PHOSPHOLIPIDE. E. OKUHARA and T. NAKAYAMA, J. Biol. Chem. **215**:295, 1955.

The structure of a methylated inositol phosphatide from soy bean lecithin is described. The authors also have evidence that glycerophosphoinositide, possessing a phosphatidic-acid-like structure, but without nitrogenous basis, also exists in soy bean lecithin. Such phosphatides may appear in brain.

PAGE, Cleveland.

DIFFERENTIAL EFFECTS OF LESIONS OF THE MEDIODORSAL NUCLEI OF THE THALAMUS ON NORMAL AND NEUROTIC BEHAVIOR IN THE CAT. C. PECHTEL, J. H. MASSERMAN, L. SCHNEINER, and M. LEVITT, J. Nerv. & Ment. Dis. **121**:26, 1955.

In order to investigate the hypothesis that degeneration of the thalamic mediodorsal nuclei is in large part responsible for the effects of prefrontal lobotomy, the effects of injury of the mediodorsal nuclei on normal and experimentally induced neurotic behavior were studied. Nine cats were trained to make discriminations and execute tasks in order to obtain food rewards. After successful training, neuroses were induced in the animals by applying shocks when they sought food rewards. These behavioral changes consisted of inhibition of feeding, phobias, and stereotyped behavior. Eight cats were similarly trained but were not then subjected to the conditioning shocks. Lesions were made stereotaxically (histologically confirmed) in the mediodorsal nuclei of the thalamus. Postoperatively the animals showed extensive amnesia for previous learning. In general, the cats with the "neurotic" behavior lost their previous restlessness and autonomic reactivity and aversion to the laboratory situation. There was an indifference to odors, including those which had previously elicited phobic reactions. Learning ability diminished, and the animals persisted in inefficient adaptive efforts to obtain food. Postoperatively, the normal cats sought out other cats or food, but the neurotic cats were immobile, attempted to hide, and attacked other cats.

BERLIN, New York.

THE CINGULATE GYRUS IN RELATION TO CONSCIOUSNESS. M. A. KENNARD, J. Nerv. & Ment. Dis. **121**:34, 1955.

Kennard studied the effects of bilateral ablation of the limbic area of the frontal lobe in cats and monkeys. In cats this cingulate ablation altered consciousness, so that the animal became less aware of its surroundings. The animal was slow and hypomotile and maintained bizarre positions for minutes or hours. Maintenance of this abnormal posture was not evident when the lesion of the frontal lobe was rostral to the cingulate area. Cats with cingulate lesions have dilated pupils, purr loudly and inappropriately, and growl in response to minor stimuli. Monkeys become passive and appear unresponsive to their environment following cingulate ablation. The additional ablation of the frontal lobes results in greater distractibility and preseverative behavior. Ablation of the temporal poles also accentuates the symptoms of cingulate ablation.

BERLIN, New York.

PATHOPHYSIOLOGIC INTERPRETATION OF THE SYMPTOMS OF RABIES. H. GESTAUT and G. MILETTO, Rev. neurol. **92**:5, 1955.

The authors attempt to explain the behavior of animals and humans suffering from rabies in the light of their observations of stimulation and ablation of the rhinencephalon. They observed that stimulation of the rhinencephalon resulted in respiratory changes, with a diminution of the rate and amplitude of respiration, coughing, sniffling, and sighing. Other autonomic effects of rhinencephalic stimulation consisted of hypotension without alteration of cardiac rate; increased or decreased peristalsis; increased lacrimal, nasal, and salivary secretions; mydriasis, and piloerection. There were also evoked movements of the facial muscles; rotation of the eyes, head, and body, and, ultimately, an adversive movement of the whole body. Bilateral stimulation resulted in a generalized spasm. In the cat, stimulation induced an arrest of current activity and assumption of a posture of attention or orientation.

Movements were evoked which indicated a reaction to some sensation in one of the extremities, as well as movements associated with eating and bowel and bladder emptying. Ablation of the rhinencephalon bilaterally was followed by coma, then prolonged sleep and narcoleptic attacks. During the waking state the animal exhibited excessive and inappropriate activity and repeatedly put objects, such as burning paper, in its mouth. There was also excessive and poorly organized sexual activity. Ablation altered the sleeping-waking pattern.

BERLIN, New York.

Neuropathology

FATAL TOXIC ENCEPHALITIS OCCURRING DURING IPRONIAZID THERAPY IN PULMONARY TUBERCULOSIS. R. S. MITCHELL, Ann. Int. Med. **42**:417, 1955.

Iproniazid, the isopropyl derivative of isonicotinic acid hydrazine, is reported by the author to have caused a fatal toxic encephalitis in a 60-year-old patient suffering from tuberculosis.

The drug was administered in daily doses of 4 to 5 mg. per kilogram of body weight, and approximately six months after treatment was initiated the patient complained of coarse tremors of both hands, tinnitus, mental confusion, and visual hallucinations. He gradually lapsed into coma and died.

Gross examination of the brain revealed numerous punctate hemorrhages in the cortex of the parietal and frontal lobes. Microscopic examination showed perivascular hemorrhages in the cortex and brain stem, as well as mononuclear infiltration in these areas.

The author believes that death may have occurred because of the acute nicotinamide deficiency which was induced by iproniazid therapy.

MANDEL, Philadelphia.

SENILE PLAQUES AND CEREBRAL ARTERIOSCLEROSIS. A. ARAB, Rev. neurol. **91**:22, 1954.

In order to evaluate the relationship of senile plaques to cerebral arteriosclerosis, the author examined 151 brains affected by arteriosclerosis, 146 brains free of arteriosclerosis, and a group of brains with only moderate arteriosclerosis. All specimens were from persons 65 years of age or older. The incidence of senile plaques was about the same in the group with as in the group without cerebral arteriosclerosis. Furthermore, the concentration of senile plaques increased diffusely with increasing age in all groups. These observations indicate that the development of senile plaques and that of cerebral arteriosclerosis are not related.

BERLIN, New York.

LESIONS INDUCED BY INTRACEREBRAL IMPLANTATION OF RADIOACTIVE GOLD. J. D. AJURIAGUERRA, P. BENDA, J. CONSTANS, M. DAVID, and M. TUBIANA, Rev. neurol. **91**:260, 1954.

Radioactive gold was inserted stereotaxically in various sites of the white matter, near the lateral ventricle and in the vicinity of the hypothalamus of cats and dogs. The animals were then killed from six days to three months later and the brains examined. The extent of the lesions varied from 3 mm. in diameter, with a dose of 0.5-5 mc., to 8 mm., for 40 mc. The lesions were spherical or distributed along lines of tracts, as in the internal capsule. They showed a central acellular zone of necrosis, with thickened vessels, surrounded by amorphous substance. Surounding the central zone was a vascularized area with perivascular infiltration. There was a dense astrocytic proliferation. At the periphery of the lesions there was considerable edema, sometimes involving the whole hemisphere. There was no clear-cut line of demarcation between the site of the lesion and the surrounding tissue.

BERLIN, New York.

Meninges and Blood Vessels

TUBERCULOUS MENINGITIS: THE DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF SPINAL FLUID SUGAR AND CHLORIDE. H. W. GIERSON and JOSEPH I. MARX, Ann. Int. Med. **42**:902, 1955.

Gierson and Marx report their observations in 231 cases of tuberculous meningitis from the standpoint of recovery based upon the spinal fluid sugar and chlorides. The chlorides were diminished with greater frequency than was the sugar. It was found that, of the two factors, the reduction of chlorides is more reliable, but neither provides a sensitive prognostic index. The authors recommend, however, that chloride determinations be continued as part of routine spinal fluid analysis in tuberculous meningitis.

MANDEL, Philadelphia.

EXPERIENCES INVOLVING THE SUPERIOR LONGITUDINAL SINUS AND ROLANDIC VEINS. H. S. SWANSON and E. F. FINCHER, Neurology **4**:801, 1954.

This study is based on seven selected cases—three cases of paramedian brain tumor in which the patent Rolandic veins were ligated at the time of tumor removal; one instance of extirpation of a patent superior longitudinal sinus with bilateral occlusion of the Rolandic venous connections; two cases of spontaneous Rolandic vein thrombosis, and a follow-up report of Dowman's case of thrombosis of the Rolandic vein, reported in 1926.

Swanson and Fincher point out that the Rolandic veins have a very important physiologic role in cerebral circulation. Disease or damage to these structures results in a classical syndrome, in some instances severer than the usual course. Ligation of the Rolandic veins can be accomplished surgically with definite anticipated neurologic results. Spontaneous thrombosis of the Rolandic vein accounts for a certain percentage of so-called "cerebrovascular accidents." The

clinical neurologic manifestations of such a condition are slow-motion reproductions of what occurs after surgical ligation of the superior cerebral vein. The prognosis for recovery without neurologic residuals in both surgical and clinical instances is much more hopeful than in occlusive arterial disease.

ALPERS, Philadelphia.

ANGIOGRAPHIC DIAGNOSIS OF VERTEBRAL ARTERY THROMBOSIS. A. VAN DER ZWAN, J. Neurol. Neurosurg. & Psychiat. **17**:189, 1954.

Van der Zwan reports two cases of thrombosis of the vertebral artery system in which carotid angiography filled the basilar artery via the posterior communicating artery. The author reports that in a series of 500 carotid angiograms he has seen only 2 other cases of filling of the basilar artery. The first was in a patient with thrombosis of the internal carotid artery; the second was that of a child with bilateral subdural hematoma.

In many cases of thrombosis of the vertebral, posterior inferior cerebellar, and basilar arteries, the clinical features are sufficient for the diagnosis. But van der Zwan suggests that in doubtful or obscure cases carotid angiography may prove helpful, not only by excluding a cerebral tumor but also by demonstrating filling of the basilar artery.

ALPERS, Philadelphia.

Diseases of the Brain

INTRACRANIAL HEMATOMAS ASSOCIATED WITH PENETRATING WOUNDS OF THE BRAIN. JOSEPH C. BARNETT and ARNOLD M. MIERKOWSKY, J. Neurosurg. **12**:34, 1955.

Barnett and Mierkowsky report the association of intracranial hematomas in penetrating injuries of the brain which occurred in Korea in 316 cases treated within eight hours by an Army Neurosurgical Unit. The majority of the wounds were caused by shell fragments from mortars, mines, grenades, or artillery fire. Fifty-one per cent of the wounds involved the left hemisphere, and the frontal and temporal lobes were involved most frequently. Of the 316 cases examined, 146, or 46%, were complicated by confined intracranial hematomas. Intracerebral hematomas were frequently encountered, as well as subdural hematomas, and the number of intracerebral hematomas increased with the number of hours elapsing between injury and treatment. The authors believe that early neurosurgical intervention will reduce this type of complication.

MANDEL, Philadelphia.

ARACHNOIDAL CYSTS OF THE CEREBELLOPONTINE ANGLE. F. G. BENGOCHEA and F. L. BLANCO, J. Neurosurg. **12**:66, 1955.

Arachnoidal cysts of the cerebellopontine angle which attain sufficient size to produce the symptoms of a tumor are rare. The authors report the case of a 51-year-old woman who had a history of a purulent discharge from the left ear 8 to 10 years before admission, followed by loss of hearing, vertigo, and signs of increased intracranial pressure. During craniotomy, a cyst was found in the cerebellopontine angle which displaced the left cerebellar hemisphere medially and reached the pons, extending rostrally to the tentorium. Microscopic examination of the cyst revealed the cyst wall to be lined by arachnoidal cells, and the wall itself was formed by a thin membrane of collagenous fibers.

The authors discuss the relationship between the cyst and the purulent discharge from the left ear, suggesting the latter as a possible etiological factor in the development of the cyst.

MANDEL, Philadelphia.

EPILEPSY WITH FETISHISM RELIEVED BY TEMPORAL LOBECTOMY. WILLIAM MITCHELL, MURRAY A. FALCONER, and DENIS HILL, Lancet **2**:626, 1954.

The authors report the case of a 38-year-old man who for 20 years had had a "thought satisfaction" when looking at a safety pin. It was highly pleasurable and much sought after by him. This would be followed by a blank period; later he made humming noises for a few seconds and sucking movements with his lips. Finally, he would stand immobile and unresponsive for two minutes. When he was 31 years old, the immobility was followed by marking time, and later by marching backward, while his right hand plucked at his left sleeve. The fits were

produced by voluntarily looking at a "bright, shiny" safety pin. Fantasies and dreams of pins were adequate as well. Sexual stimulation and anxiety-producing situations were the commonest states in which the desire to look at a pin arose.

He became impotent and had three short psychotic episodes. Examination revealed a left temporal focus on the EEG and focal dilatation of the temporal horn of the lateral ventricle. When safety pins were shown to him while the EEG electrodes were attached, frequent firing over the left frontotemporal region was observed, followed by a clinical fit.

A left anterior temporal lobectomy was performed, including the removal of the uncus and anterior part of the hippocampus. The specimen was grossly normal, but microscopically there was slight atrophy of the cortex and white matter, with compensatory gliosis.

Follow-up for 16 months revealed no further fits, no desire to look at a safety pin, and return of his sexual potency. A postoperative EEG revealed the general character to be normal and the exhibition of a safety pin did not change the record.

MADOW, Philadelphia.

Diseases of the Spinal Cord

INTRASPINAL TERATOMA, WITH REPORT OF A CASE. E. S. HARRINGTON and J. F. KELL JR., J. Neuropath. & Exper. Neurol. **14**:214, 1955.

Harrington and Kell report an instance of teratoma occurring in the spinal cord. A 13-year-old girl complained of gradually increasing lumbosacral pain and difficulty in walking for three months prior to admission. Weakness in the lower extremities was noted in the extensor and peroneal muscles and in the hamstrings and quadriceps, gastrocnemius, and soleus muscles. There was anesthesia of the lateral aspect of the left foot and hypesthesia of the right foot and leg below the knee. The muscle stretch reflexes were active, and the Babinski sign was present. Plain roentgen films of the spine showed compression and anterior triangulation of the 5th thoracic vertebra, erosion of the pedicles of the 9th through the 11th thoracic vertebrae, and widening of the corresponding interpeduncular spaces. Lumbar puncture yielded xanthrochromic fluid, containing 2800 mg. of total protein per 100 cc., with an occasional polymorphonuclear leucocyte and lymphocyte. Evidence for a partial block of the subarachnoid space was noted with the Queckenstedt test. An iophendylate (Pantopaque) myelogram indicated a mass at the lower level of the 12th thoracic vertebra. Laminectomy from the ninth thoracic to the second lumbar disclosed an enlargement of the spinal canal and dura in both diameters, extending along the canal for a distance of 4.5 cm. The tumor weighed 12.6 gm., and its surface was irregularly lobulated from thin-walled cysts. Microscopic examination revealed a cystic, organoid tumor, composed of several embryonic elements, most striking of which were mature adipose tissue, smooth muscle, mesenchymal tissue, imperfect glomeruli and Fallopian tubes, thyroid, and a variety of secretory glands. Little or no improvement was noted following the operation.

SIEKERT, Rochester, Minn.

Peripheral and Cranial Nerves

PULSELESS DISEASE: CENTRAL NERVOUS SYSTEM MANIFESTATIONS. R. D. CURRIER, R. N. DEJONG, and G. G. BOLE, Neurology **4**:818, 1954.

The authors describe a case of complete occlusion of all the arteries arising from the arch of the aorta. A summary of the symptoms in 40 reviewed cases of pulseless disease indicates that the commonest symptoms were visual, 32; syncope and loss of consciousness, 29; dizziness and vertigo, 19; headache, 17; paralysis, 15; sensory changes, 10; convulsions, 9; aphasia, 8; carotid sinus sensitivity, 9, and bulbar signs, 5.

The commonest known cause of the aortic arch syndrome is syphilitic aortitis with aneurysm. Several reports of this syndrome have included a high incidence of young women with negative tests for syphilis, in whom the pathologic picture was that of a nonsyphilitic chronic arteritis. Other suggested etiologies have been embolism, extravascular mediastinal tumors, and thrombophilia.

Treatment in most cases has had little effect on the course of the disease. If proved to be present, syphilis should be treated. Such therapy has seemed to have halted the disease process in some cases. Various surgical techniques have been attempted. The results of these procedures have been equivocal.

ALPERS, Philadelphia.

RETICULOSIS OF THE NERVOUS SYSTEM SIMULATING ACUTE INFECTIVE POLYNEURITIS. R. S. ALLISON and D. S. GORDON, Lancet **2**:120, 1955.

Allison and Gordon report a case of the Guillain-Barré syndrome which developed rapidly in a 56-year-old woman. The cerebrospinal fluid showed increased protein. The patient had mental symptoms.

Necropsy revealed widespread reticulosis, with a large deposit in the right cerebral hemisphere and diffuse microscopic infiltration of the midbrain, leptomeninges, and spinal nerve roots. The authors discuss the question whether the clinical signs, which resemble those of polyneuritis, were "toxic" or mechanical in origin. Polyneuritis occurs with relative frequency in cachectic conditions and in malignant disease, and most of these cases, rightly or wrongly, are regarded as "toxic." In the present case the malignant changes found outside the nervous system did not involve any organ whose loss of function might have favored the development of toxic polyneuritis. The nerve roots were infiltrated with tumor cells, and it appears probable that the paralysis of the lower limbs and the cranial nerve lesions were purely mechanical effects. Microscopic examination of the invaded tissue revealed a reticulum-cell sarcoma.

YASKIN, Camden, N. J.

OPTIC NEURITIS FOLLOWING ISONIAZID THERAPY. J. A. KEEPING and C. W. A. SEARLE, Lancet **2**:278, 1955.

Keeping and Searle report the development of optic neuritis 25 days after the administration of isoniazid, with subsequent improvement despite late withdrawal of the drug. They indicate that isoniazid may be a toxic agent. This complication is fortunately rare, and an idiosyncrasy may perhaps be the precipitating factor.

YASKIN, Camden, N. J.

Treatment, Neurosurgery

SYDENHAM'S CHOREA: II. EFFECTS OF HORMONE THERAPY. L. E. AINGER, R. S. ELY, A. K. DONE, and V. C. KELLEY, A. M. A. Am. J. Dis. Child. **89**:580, 1955.

Evidence suggesting the existence of a state of relative adrenal insufficiency in patients with Sydenham's chorea had previously been presented. Also, a state of relative adrenal insufficiency has been shown to exist in patients with active or inactive rheumatic fever. Since corticotropin and cortisone have been reported to be efficacious in therapy of exudative rheumatic fever, and since similar biochemical and physiological abnormalities occur with these two diseases, it seemed logical that hormone therapy might be of value in chorea.

The authors treated 11 patients with 13 attacks of Sydenham's chorea. Two of the patients had recurrences, who received a second course of hormone therapy. In general, corticotropin was administered intramuscularly in a daily dose of 0.9 to 2.0 I. U. per pound of body weight. The patients were maintained on bed rest, and all but one received large daily supplemental doses of ascorbic acid and all received daily penicillin prophylaxis. The patients received the initial daily dose of corticotropin until clinical improvement appeared to be maximum, and then the dose was tapered gradually over a period of about a week. Six patients had clinical, electrocardiographic, or fluoroscopic evidence of carditis. In all these the erythrocyte sedimentation rate was elevated during the pretherapy period.

In most of the cases initial improvement in the chorea occurred within the first week of therapy. In five patients the response was classified as dramatic. For instance, one patient who had required a padded crib for prevention of bodily harm from the constant choreiform movement improved so much within three days that he was able to walk, talk, and feed himself. Only one patient in this series failed to show definite response to therapy, and this one did not receive ascorbic acid. The authors suggest that ascorbic acid may function in the peripheral utilization of the 17-hydroxycorticosteroids. Evidence has been recently reported that hormone therapy appears to be effective in preventing residual cardiac damage in patients with rheumatic carditis. However, the number of patients with chorea who have been treated with hormones is too few, and the period of follow-up too short, to permit any evaluation of the effect of this therapy on the final cardiac status. (The delayed appearance of rheumatic heart disease, especially "pure" mitral stenosis, is not an infrequent occurrence in patients whose only symptom has been Sydenham's chorea.)

It is the authors' feeling that patients with chorea should be treated as those with rheumatic fever and placed on sulfonamide or penicillin prophylaxis and put at bed rest.

SIEKERT, Rochester, Minn.

TREATMENT OF TIC DOULOUREUX BY BLOCK OF SECTION OF THE GREAT AURICULAR NERVE. A. ROWLAND, A. M. A. Arch. Otolaryng. **61**:549, 1955.

The author has found that by injection of the great auricular nerve with alcohol or by section of this nerve the pain from trigeminal neuralgia was greatly relieved. The basis of the operation is the physiological fact that there is a marked and constant overlapping in the sensory area of the head and neck of many of the spinal nerves with the cranial nerves. The great auricular nerve, being an entirely sensory nerve, has fine terminal ramifications in the entire region, which is also innervated by the sensory supply of the trigeminal nerve. In addition, the great auricular nerve is easily accessible over the sternocleidomastoid muscle, in comparison with the more difficult and dangerous intracranial approach to the Gasserian ganglion. This method also eliminates some of the complications of trigeminal ganglion injections, such as pain in the face or ectropion of the lower eyelid.

MANDEL, Philadelphia.

Books

Lobotomy: A Clinical Study. By A. Miller. Price, not given. Pp. 107, with 29 figures and 53 tables. Ontario Department of Health, Toronto, 1954.

In this volume is reported a detailed clinical and laboratory study of 150 patients with mental disorders subjected to lobotomy at the Toronto Psychiatric Hospital during the years 1948 to 1952. The objective was to determine what factors were predictive of a good result. There were many good results; indeed, 55% of the patients were out of hospital and functioning reasonably well a year after operation. Since the patients had been hospitalized for an average of five years, these clinical results are outstanding. However, there was no single item, and, indeed, no group of items, that made for any very reliable prognosis. Even duration of hospitalization was considered of no great importance. This factor is suspect, however, since so few of the patients were operated upon before the five-year period had elapsed. Prediction was based upon a quantitative scale, where zero represented the patient who was a constant nursing problem, 50 the patient who was out of hospital, unsupervised but not working, and 100 the patient who had no psychotic residuals and who was functioning at a high level socially. Preoperatively most of the patients were at the zero level, and none above 30 points, so that improvement was considerable in most instances. However, the question of which patient would respond favorably to operation and which patient would not improve was much more difficult to forecast. "For practical purposes, it can be said that the predictive assessment was good in 54 patients or 48%. The predictive rating was too high in 32 patients or 28%, with the majority of cases being assessed incorrectly from 20 to 40 points, and in a few cases there was a greater inaccuracy (the highest being 60 points). The predictive rating was too low in 27 patients or 24%; and again, in the majority of cases the margin of predictive error was 20 to 40 points, with a few showing wider range of inaccuracy." Unfortunately for future efforts in prognosis, this predictive assessment showed no greater accuracy in the 1952 series than it did in the earlier ones. The author went back over his material and tried for better criteria on the basis of actual accomplishment, but, aside from such definite factors as operative hemorrhage and other organic complications that lower very markedly the anticipated outcome, there were so many instances in which unexpectedly good results occurred in apparently hopeless cases, and vice versa, that the subject is still open.

Special studies in great array revealed that periodic attacks of mental illness were apt to respond with reduction of the swings from one stage to the other. Tension was reduced or eliminated in all but five patients; two-thirds of the patients gained weight; 95% slept well, and 50% did not dream. Nine patients showed abnormal increase in sex drive, attributable either to prepsychotic behavior or to postoperative organic disturbance with reduced social capacities. Many other patients enjoyed freer expression of normal sexuality because of "a reduction of anxiety and guilt previously associated with sexual urges and experiences." Glucose tolerance curves failed to show any significant changes resulting from lobotomy. Hallucinations disappeared in 50% of the patients and delusions in 40% of the patients who experienced them before operation. No patient developed these phenomena anew after operation. Eight of the 18 patients with persistence of symptoms benefited from electroconvulsive shock.

Miller noted the following personality changes after operation: temporary apathy and reduced initiative; reduced planning ability; reduced social sensibility; outwardly directed behavior; lowered range of feeling tone; retention of skills and intellectual functioning, and particularly, a "marked tendency towards gratifying pleasurable needs, with short-lived irritability when these pleasures were thwarted." There were 3 operative deaths, 2 cases of hemiplegia, 7 cases of dementia, 9 cases of epilepsy, and 16 cases of prolonged incontinence—not a bad incidence for 150 patients.

Further studies of patients revealed that the following factors were of little predictive value: constitutional predisposition, age, sex, duration of illness, and precipitating factors. On the other hand, the prepsychotic personality and the response to shock therapy were of some predictive value. Clinical features developing during the psychosis were among the most reliable prognostic guides, but even so there were many instances, as noted above, where the clinical features could be misleading. Electroencephalographic studies before lobotomy showed that those patients with an occipital alpha rhythm of 9 to 11 cps were neither good nor bad risks, while those between 7

and 9 cps were all good risks, and most of those above 11 cps were bad risks. Poor organization of the alpha rhythm was indicative of a poor result. The well-known large slow waves in the frontal region following lobotomy were substantiated. "The component of the EEG most markedly affected by lobotomy was the amount of alpha waves."

A battery of psychologic tests was administered to 61 patients before and after lobotomy, with the following results: Greater improvement was found to be associated with an I. Q. above 100, higher Performance than Verbal scores, a small degree of Performance scatter, and relatively high scores on Picture Completion, Picture Arrangement, and Similarities subtests of the Wechsler-Bellevue Scale. On the Rorschach test absence of anatomy responses and presence of human movement were of good prognostic implication. Comparison of preoperative and postoperative Wechsler scores disclosed few significant findings. Technical aspects, both surgical and nursing, are included, and representative case histories in the various categories complete this handsomely printed monograph, replete with charts in color.

The Kidney: Ciba Foundation Symposium. By A. A. G. Lewis, M.D., M.R.C.S. Edited for the Ciba Foundation by G. E. W. Wolstenholme, O.B.E., M.A., B.Ch.; assisted by Joan Etherington. Price, $6.75. Pp. 333, with 125 illustrations. Little, Brown & Company, 34 Beacon St., Boston, 1954.

This informal symposium on renal problems is another one of the series initiated by the distinguished Ciba Foundation, London, Trustees, Prof. E. D. Adrian, Lord Beveridge, Lord Horder, and Mr. Raymond Needham, and on this occasion carried out in collaboration with the Renal Association. The multiple stimuli received by the reviewer must be shared by many other readers, for, again, one feels cogently the fluidity of many questions of structure and physiology, and many tenets complacently held, neatly torn asunder, usually with the quietude accorded to the division in two of a soggy newspaper, but no less annihilating. Twenty-two papers were presented, and although one cannot divorce formal readings from the organization of medical literature, the give and take of each discussion always seems to come as a fresh northern breeze to the hot wilted city during summer's terrible heat.

Unfortunately, great detail cannot be entertained in discussing the many superior papers in this symposium, and the discussion itself always includes many small gems. There was support for the hypothesis that there is a hypertonic zone in the medulla of the kidney, with hypertonic glomerular filtrate formed in the loops of Henle with a concentration ingredient as one traverses the same loops with avoidance of osmotic gradients. Dr. Jean Oliver's dissection technique of nephrons came in for some great usefulness by Dr. E. M. Darmady in the Fanconi syndrome with the demonstration of a long swan-like neck of tubule between the glomerulus and the normal part of the proximal tubule. There was additional material for support of a technique of aspiration biopsy of kidney tissue by Dr. F. Raaschou, of Copenhagen. Dr. Jean Oliver describes recovery from acute tubular necrosis, in which he places two types of lesions: a tubulorrhexis, with tubular rupture at any level, and a nephrotoxic lesion, with tubular cells destroyed by preservation of the epithelial membrane. He relates regeneration of these epithelial cells to an intracellular maturation, with particular reference to the enzymatic activity centering around the mitochondria. Further evidence to show that renal glycosuria was not in itself a clinical entity was presented by Dr. Reubi, of Bourne. Investigative work coming from Columbia University by Drs. S. E. Bradley and J. Taggart revealed that the specific activity of urine might be higher than that of the corresponding plasma; they used a technique of C^{14}-labeled urea, and further studies using P. A. H. transport in kidney slices revealed that this transport was coupled with respiration, and dependent, as might be expected, on phosphate-bound energy. It was deduced that the carboxyl group of P. A. H. must interact with some definite intracellular element in the transport system, and undoubtedly coenzyme A is one of these links. Another portion of the symposium was related to the regulation of acid-base balance, and in this particular group of papers there is an interesting hypothesis developed by Dr. R. F. Pitts, of Cornell University, that in the presence of a high arterial pCO_2 the hydration of CO_2 intracellularly within the tubule took place more rapidly and there was an increase in available hydrogen ions for exchange with base, thus conserving base for the body: This effect thus counters that of inhibition of carbonic anhydrase by infusing carbonic anhydrase inhibitor (otherwise known as 606_a). Further evidence for the thesis that potassium and hydrogen ions compete for exchange with sodium ions, thus having some common step in their transport, was presented by Dr. R. W. Berliner, of Bethesda, Md. Dr. J. R. Robinson, of Cambridge University, described some data which he believes form a primary step in the ion exchange mechanism within the

tubular cells, such as perhaps sodium reabsorption with a passive diffusion into the tubular lumen of potassium or hydrogen ions, depending upon their concentration or availablity in the cell. He further indicated that even though there took place a very small exchange of hydrogen ion for the base, if some buffer were available there would then be established a very high gradient, and intracellular ammonia would then diffuse out to bind hydrogen ions, permitting further hydrogen ion exchange for base.

Electrolyte excretion came in for some discussion, and Dr. C. E. Dent presented evidence, in contradistinction to Fuller Albright and his group, that only a slight phosphorus excretion increase took place when normal subjects were treated with parathyroid hormone. Further excellent contributions on electrolyte excretion were made by Dr. Neils Elwald, of Lund; J. P. Merrill, of Boston, and A. A. G. Lewis, of Middlesex Hospital, London. The final section of the symposium dealt with the volume control of body fluid, and summarization of the present views on the excretion of water, sodium, and potassium was presented.

Usefulness of such a symposium certainly is not restricted to the renal physiologist, but, rather, spreads out into the vast domain of all physicians, from dermatologists to neurosurgeons, interested in renal problems and their widespread effects on the rest of the body.

Truants from Life: The Rehabilitation of Emotionally Disturbed Children. By Bruno Bettelheim. Price, $6.00. Pp. 511, with illustrations. The Free Press, Glencoe, Ill., 1955.

This volume is the second of a planned series of three about the work of the Sonia Shankman Orthogenic School of the University of Chicago. The school is a residential treatment institution devoted to the rehabilitation of children with very severe emotional disturbances, to research into the causation and treatment of these disturbances, and to the training of persons who wish to teach and treat such problem children. The first book, "Love Is Not Enough," presented the school's educational and therapeutic philosophy, using as examples, in an incomplete and scanning fashion, the specific problems and methods of the school. The third volume will deal with the staff and the school as a social organism. The present book, however, attempts to describe the actual workings of the school, by taking four separate case histories of severely disturbed children, presenting something of their background, and taking them step by step through their life and work in the school, and includes follow-up material after discharge. Each case may be read separately. Included are direct quotations from the children about themselves and the school psychological test reports and responses, drawings, and a series of statistics about the children and their parents. From all of this one derives a very clear picture of the problems encountered and the methods developed to deal with this most difficult of groups: the children so severely disturbed socially and emotionally that they must be institutionalized. Most children had had attempts at psychoanalysis, psychotherapy, or institutionalization before coming to the Orthogenic School, with little or no success. All four cases presented were gratifyingly improved on discharge, after three to seven years of treatment.

As the cases unfold, one sees the tremendous thought and planning that has gone into the creation of the school's therapeutic milieu, in which intense attempts are made to understand, accept, and help the child to modify his own behavior when he himself is ready. With certain obvious limitations, each child has his own treatment setting, with freedom to regress, to test, to grow, to progress. Bettelheim stresses the children's need "to learn to seek and find security in the intimacy of human relations." He describes clearly how the rehabilitation of each child actually proceeds.

Although much of this is reserved for the next volume in the series, there is considerable material about the counselors and staff of the school, dealing with the kinds of people (and their problems, too) who can handle these jobs and thrive on them. There is a great deal of awareness of the transactional processes functioning between child-counselor, child-child, and child-parent.

There is much in this book that will be of value to those who work in other institutions, and to all those who deal with any kind of child in any capacity whatsoever. As Bettelheim states, "Those who have been able to participate directly in the unfolding of an integrated personality where formerly there was none, who have helped to liberate a mind so frozen it seemed not to exist—those who have watched closely the emergence of human relations, positive emotions, and enjoyment of life where before there was nothing but defiant or hopeless isolation, hatred, angry anxiety, or homicidal violence—will experience a greater conviction about the efficacy of our methods than could be derived from any statistical treatment."

Management of Addictions. By Edward Podolsky, Editor. Price, $7.50. Pp. 413. Philosophical Library, Inc., 15 E. 40th St., New York, 1955.

This volume is a collection of thirty-five papers by forty-eight authors, dealing with various aspects of alcoholic and drug addictions. All papers have been previously published elsewhere.

The book is divided into two sections, the first dealing with alcohol addiction. Excessive drinking and chronic alcoholism are differentiated. The latter is seen as a multifactorial problem with compound etiology. Some authors feel that alcohol is used to diminish tensions related to early oral deprivation; others feel it can be used as a defense against tension due to any type of problem, in persons generally intolerant of stress. There are several papers about alcoholism as a genetotrophic disorder, that is, a nutritional deficiency with an inherited partial enzymatic block.

Therapies ranging from acute management to chronic care, and from Alcoholics Anonymous and Antabuse to calcium injections and carbon dioxide, are presented and evaluated. A plea is made for a multifocal constructive teamwork approach, with supportive and directive psychotherapy as one facet. Sociologic and psychological factors are taken into consideration. In no paper is psychoanalytically oriented psychotherapy, specifically dealing with those conflicts that have engendered the original tensions, felt to be of primary importance or value.

The second section includes nine papers on other drug addictions. Group psychotherapy, EST, calcium therapy, and prolonged sleep are discussed. The value of education of the addict is apparent. The final paper concludes with some thought-provoking remarks on prevention of public exposure to addicting drugs.

This book is of value primarily to those physicians who are actively engaged in the medical care of addicted persons.

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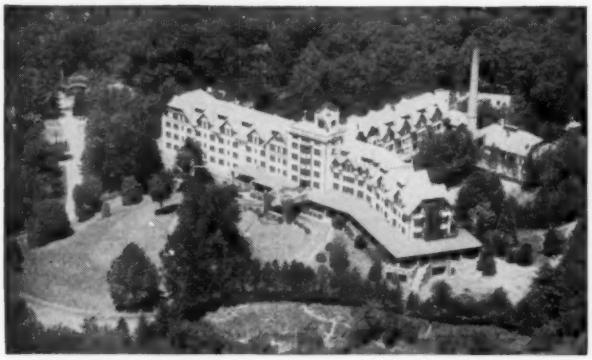

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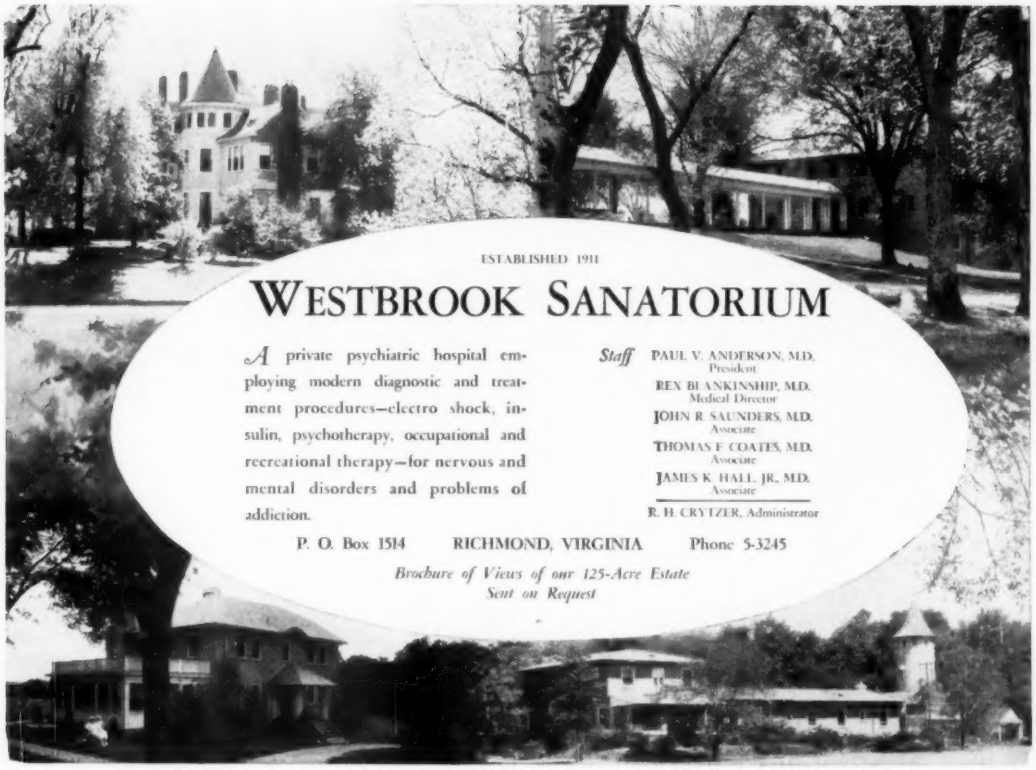

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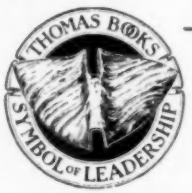
THE ULTIMATE OBJECTIVE OF NEUROCHEMISTRY, in partnership with Neurophysiology and Neuropathology, is the understanding of the phenomena underlying the behaviour of nerve, brain and mind, and the maladies to which they are subject. THE FURTHERANCE OF THIS UNDERSTANDING IS THE AIM OF THIS WORK.

The authors give, for the first time, an account of our present knowledge of the chemistry of the nervous system and its bearing on neurological phenomena. It is written for a wide circle of investigators and students, for the biochemist and the physiologist, for the neurologist, neuropathologist and the neurosurgeon, for the clinician, the pharmacologist; indeed, for all interested in the workings in the nervous system, whether it be in man or in the insect.

Here are described the chemical constituents of brain and nerve, the factors influencing respiration and other metabolic phenomena of the nervous system, the effects of narcotics and convulsants, venoms and nerve poisons.

The biochemistry of the brain during its early development, the composition and behaviour of intracranial fluids, the significance of acetylcholine in nerve physiology, nutritional, genetic, and behavioural disorders in the nervous system, and neuromuscular diseases,—all these and a variety of other topics are discussed in full.



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